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TABLE OF CONTENTS

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ORIGINAL ARTICLES.

STUDIES IN PANCREATIC FUNCTION. THE ENZYME CONCENTRATION OF DUODENAL CONTENTS IN PATHOLOGICAL CONDITIONS INVOLVING THE PANCREAS, LIVER AND STOMACH. *By Charles W. McClure, M.D.*, Boston, and *Chester M. Jones, M.D.*, Boston 909

CONGENITAL OBLITERATION OF THE BILE DUCTS AND CONGENITAL BILIARY CIRRHOSIS OF THE LIVER. *By J. Keith Gordon, M.D.*, Boston 923

THE PROBLEM OF THE TUBERCULOUS SUSPECT. *By John B. Hawes, 2nd, M.D.*, Boston 928

THE EDUCATION OF THE TRAINED NURSE. *By Channing Frothingham, M.D.*, Boston 930

EDITORIALS.

THE MEETINGS OF THE AMERICAN ASSOCIATION FOR THE ADVANCEMENT OF SCIENCE 933

PASTEUR 933

DR. BULKLEY'S RETIREMENT FROM THE NEW YORK SKIN AND CANCER HOSPITAL 934

THE ADVENT OF COUÉ 935

MESSAGE OF DR. LINSLY R. WILLIAMS TO MASSACHUSETTS 935

NEWS NOTES 936

THE COMBINED MEETING OF THE MIDDLESEX SOUTH, NORFOLK AND NORFOLK SOUTH DISTRICTS 936

INSTRUCTIVE DISTRICT NURSING ASSOCIATION, BABY HYGIENE ASSOCIATION 937

OBITUARY.

HENRY WHITMAN KILBURN, M.D. 937

MISCELLANY.

A RIFT IN THE CLOUDS 937

LOW INCIDENCE OF VENEREAL DISEASE IN OUR COLLEGES 938

TRYING TO LIFT THE BAN ON MALT LIQUORS 938

THE INFECTIOUSNESS OF MEASLES 938

COOK PORK WELL TO AVOID TRICHINOSIS 939

CORRESPONDENCE.

DARWINISM AND EVOLUTION—THEIR RELATION TO THE PHYSICIAN. *J. Dansforth Taylor, M.D.* 939

COMITÉ D'AIDE DE L'UNION DES AVEUGLES DE GUERRE. *Kendall Emerson* 940

NEXT MEETING OF THE AMERICAN SURGICAL ASSOCIATION. *R. B. Greenough* 941

HUMAN ACTINOMYCOSIS. *A. H. Sanford, M.D.* 941

THE TREATMENT OF PNEUMONIA. *Beverley Robinson* 941

IN MEMORIAM—LOUIS PASTEUR 941

DIABETES AND ITS SURGICAL COMPLICATIONS 942

SOCIETY MEETINGS 942

Original Articles.

STUDIES IN PANCREATIC FUNCTION. THE ENZYME CONCENTRATION OF DUODENAL CONTENTS IN PATHOLOGICAL CONDITIONS INVOLVING THE PANCREAS, LIVER AND STOMACH.

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NUMEROUS clinical studies[1] have been made of enzymatic activity in the stools, urine and duodenal contents, in an effort to obtain a satisfactory measure of the activity of the external secretory function of the pancreas. The results of such investigations have led observers to maintain that obstruction of the pancreatic duets is accompanied by marked diminution in proteolytic, amylolytic and lipolytic activity in duodenal contents, and in the amylolytic activity in stools, while the amylolytic activity in urine was observed to be increased. Critical examination of the methods used in all such studies, however, has shown them to be far from accurate, and subject to large degrees of individual error. By such methods it was demonstrated that the amylolytic activity in both urine and stools varied greatly in persons without pathological involvement of the pancreas, and diagnostic deductions based upon such estimations were of little or no clinical significance.[2]

The relative inaccuracy of all methods for estimating enzymatic activity, that have been employed in studying cases of supposed pancreatic insufficiency, is recognized. The fallacy of drawing conclusions from data obtained by them rendered desirable the development of newer methods, which would conform with the present-day concepts of the physical chemistry of enzyme action. The recent work of McClure, Wetmore and Reynolds[3] has made possible the application of more refined technic to the study of external pancreatic function, and has eliminated many of the obvious sources of error in previous methods. The methods devised by these investigators conform to the newer concepts of enzyme action, and they take into account certain previously disregarded factors, such as the influence of buffer conditions and of hydrogen ion concentration on enzyme action, lack of uniformity of enzymatic activity, lack of stability of enzyme action, etc. These workers studied, by means of these methods, a series of fifteen normal individuals,[4] determined the approximate accuracy of the methods, and found the normal variation and lower normal limits of enzyme action in the duodenal contents. These findings were later cofirmed by further observations on normal persons and patients without demonstrable pancreatic disease.*

*Unpublished observations.

It is the purpose of this paper to present the findings obtained by the use of the above methods as applied to a series of selected cases, consisting largely of acute or chronic involvement of the pancreas or biliary tract. We shall attempt to consider, first, the pathologic physiology existing in cases of pancreatic disease, and second, the practical clinical value of the above tests of enzymatic activity, as a means of diagnosis and prognosis. Studies of the enzymatic activity in the duodenal contents have been made in patients with pernicious anemia, achylia gastrica, chronic colitis, carcinoma of the liver and bile ducts, carcinoma of the pancreas, acute and chronic pancreatitis, and in patients with jaundice from other causes.

Technic.—The method of procedure for obtaining duodenal contents has been described in a previous article.[4] In brief, it consists in allowing the duodenal tube to pass into the second portion of the duodenum and verifying its position by fluoroscopy. The patient then drinks a mixture consisting of 40 c.c. of 20 per cent. cream (ordinary heavy cream) in which is suspended 15 grams of barium sulphate. The barium is added because it has been found that cream often appears in the duodenal contents more quickly when mixed with barium than when given alone. After ingesting the cream and barium mixture the patient lies on the right side, and the flow of duodenal contents is initiated by gentle suction with a syringe. As soon as the flow has started, the duodenal contents are allowed to siphon off, and are collected for one hour after barium appears in the duodenal contents.

The estimation of enzymatic activity is made, within an interval of not more than eighteen hours after collecting the duodenal contents, by the methods devised by McClure, Wetmore and Reynolds.[3] How much longer than eighteen hours the enzymes remain stable has not been determined. Proteolytic activity is estimated by allowing a dilution of the duodenal contents to act on a solution of soluble casein. The casein not affected by proteolytic action is precipitated by means of metaphosphoric acid solution. The index of proteolytic activity is taken as the number of milligrams of nitrogen not precipitated by the metaphosphoric acid. This nitrogen value is determined by an adaptation of the method of Folin and Wu for the determination of non-protein nitrogen in the blood. Amylolytic activity is estimated as the number of milligrams of glucose developed by action of duodenal contents on a solution of soluble starch. The index of amylolytic activity is taken as the total number of milligrams of glucose developed, as determined by the method of Folin and Wu for the determination of sugar in the blood. Lipolytic activity is estimated by allowing duodenal contents to act on a true emulsion of cottonseed oil, and determining the amount of acidity developed by titrating with tenth normal alcoholic solution of NaOH. The total number of c.c. of N/10 NaOH necessary to neutralize the acidity developed is used as the index of lipolytic activity. The samples of duodenal contents and the reagents used must be controlled for the presence of nitrogen not precipitated by metaphosphoric acid, for copper reducing bodies and for acidity. In a certain number of cases it was found that the duodenal contents obtained both from patients and from

Table 1

Enzymatic activities, amounts and physical character of duodenal contents in achylia gastrica, pernicious anemia and chronic colitis.

Case No.	Enzymatic Activity			Amt. in c.c.	Color	Viscosity	Diagnosis
	Proteolytic in mgm. NPN	Lipolytic in c.c. N/10 NaOH	Amylolytic in mgm. glucose				
Control	2.0	1.0	1.0	50 to 400	greenish yellow	moderate	Minimum normal limits
1.	2.8	1.4	2.0	105	lemon yellow	moderate	Achylia gastrica
2.	3.7	2.6	4.7	70	greenish yellow	moderate	Achylia gastrica
3	3.3	1.6	3.8	150	greenish yellow	moderate	Pernicious Anemia
4.	5.0	2.5	3.1	150	greenish yellow	moderate	Pernicious Anemia
5.	3.0	1.6	2.0	150	greenish yellow	moderate	Chronic Colitis

normal subjects were so viscid that pipetting was difficult. The results obtained, however, in examining such specimens were entirely comparable to those obtained in cases in which the viscosity was not excessive. The extremely viscid duodenal contents were diluted as called for by the method for estimating amylolytic activity, and filtered through dry filter paper. With this precaution the final blue solution was not turbid.

Examination of Cases.—The enzymatic activities of duodenal contents obtained from four patients with achylia gastrica were estimated. Two of these patients presented the clinical entity achylia gastrica, with chronic diarrhoea, and two, pernicious anemia in severe relapse. A fifth patient was studied who was suffering with chronic colitis. The findings in these cases, together with the minimum normal limits of enzymatic activity in duodenal contents as determined in normal individuals, and in patients without pancreatic disease, are outlined in the following table (Table 1). Study of these results show that the activities of the various types of enzymes in the duodenal contents were well above the minimum normal limits. The significance of these findings will be discussed later.

The enzymatic activities in the duodenal contents obtained from patients with some form of pancreatic disease were next studied. The findings are outlined in Table 2. All but two of the patients included in this group underwent an exploratory laparotomy during their

Table 2

Enzymatic activities, amount and physical character of duodenal contents obtained from patients with disease of the pancreas.

Case No.	Enzymatic Activity			Amt. in c.c.	Color	Viscosity	Diagnosis
	Proteolytic in mgm. NPN	Lipolytic in c.c. N/10 NaOH	Amylolytic in mgm. glucose				
6.x	3.6	1.0	1.2	150	greenish yellow	moderate	Pancreatic Cyst
7.x	2.5	1.4	2.0	90	greenish yellow	moderate	Cancer of tail and body of pancreas; diabetes mellitus
8.	0.9	0.0	0.0	55	white	very great	Cancer head of pancreas
9.x	0.0	0.2	2.0	100	white	very great	Cancer head of pancreas
10.x	3.0	1.6	1.4	150	greenish yellow	moderate	Chronic cholecystitis, cholelithiasis, acute pancreatitis
11.x	0.8 1.1	0.3 0.3	0.3 0.5	50 60	yellow yellow	great great	Chronic cholecystitis, cholelithiasis, chronic pancreatitis
12.a	1.6	0.4	0.5	250	greenish yellow	moderate	Hemochromatosis Chronic pancreatitis
13.x	0.0	0.0	0.0	105	yellow green	moderate	Chronic pancreatitis, diabetes
14.x	1.9 5.0	0.7 0.2	1.9 0.4	150 100	greenish yellow	moderate moderate	Acute pancreatitis, acute cholecystitis
15.x	1.7	0.0	0.7	130	green	very great	Acute pancreatitis
	0.9 3.2 0.5	0.0 0.8 0.2	0.0 0.5 0.1	150 100 100	yellow green-yellow yellow	moderate " "	
16.	2.6	1.0	1.2	100	green-yellow	"	Diabetes Mellitus

x-exploratory laparotomy. a-autopsy

stay in the hospital, or were examined at autopsy. Of the two cases not so examined one was clinically cancer of the head of the pancreas, and the other was a case of severe diabetes mellitus.

In Table 2 the enzymatic activities of the duodenal contents from Cases 6, 7, 10 and 16 were above the minimum normal limits. The duodenal contents in Cases 6, 7 and 10 were obtained about two weeks after laparotomy. Case 6 was one of cyst of the pancreas. The situation of the cyst was such that there was very little involvement of the pancreatic parenchyma, and no obstruction of the duct of Wirsung. At laparotomy in Case 10 two necrotic areas were found on the surface of the pancreas, but the greater part of the pancreatic parenchyma was not demonstrably diseased. Exploration in Case 7 showed the tail and body of the pancreas to be largely replaced by carcinomatous tissue. The head of the pancreas, however, was not involved, and there was no obstruction to the pancreatic duct. Case 16 represented extremely severe diabetes mellitus. The patient had lost fifty-six per cent. of his usual body weight.

The enzymatic activities of the duodenal contents of Cases 8, 9, 11, 12, 13, 14 and 15 were for the most part abnormally low. The clinical records of these cases will be found in the section of this article entitled Case Reports. Case 8 was clinically cancer of the head of the pancreas and obstruction to the pancreatic duct could explain the diminished enzymatic activity, but no operative or autopsy confirmation of the diagnosis was obtainable. Case 9 was one of carcinoma of the head of the pancreas, diagnosed at operation. The duodenal contents from this case showed negligible degrees of proteolytic and lipolytic activity, but amylolytic activity was well above the minimum normal limit. Case 11 was admitted to the hospital with a provisional diagnosis of possible pancreatic tumor. Studies of the duodenal contents showed a diminution of the three types of enzyme action. At operation chronic gall-bladder disease was found, and, also, one small stone in the cystic duct. In addition the pancreas was exceedingly hard throughout, and gave grossly the typical finding of chronic interstitial pancreatitis. Case 12 was one of hemochromatosis, with chronic pancreatitis. At autopsy it was observed that the pancreatic parenchyma was not greatly fibrosed, so that the diminished enzymatic activities found were not the result of great anatomical destruction of pancreatic tissue.

The first specimens of duodenal contents were obtained from Cases 14 and 15, about two weeks after laparotomy. Both these patients presented cases of acute hemorrhagic pancreatitis with extensive involvement of the pancreatic parenchyma. In the first specimen of duodenal contents obtained from Case 14, the proteolytic and lipolytic activities were just below the minimum normal limit, while amylolytic activity was above this limit. Nineteen days later a second specimen of duodenal contents showed proteolytic activity well above the minimum normal limit, while lipolytic and amylolytic activities were much decreased below normal. The enzymatic activities of the first specimen and of the second specimen (obtained five weeks later) from Case 15, were both below the minimum normal limits. A third specimen was procured two weeks after the second. The proteolytic activity in this third specimen was above the minimum normal, lipolytic activity was slightly reduced, and amylolytic activity was much below the normal. The fourth specimen was taken five months after operation. The patient was in fair physical condition, but the examination of the duodenal contents showed a further decrease in all the enzymatic activities. In both these cases it was found that in the same specimen of duodenal contents one type of enzymatic activity was above the minimum normal limit, while the other two types were below this limit, and that the discrepancy was well marked.

Case 13 was one of unusual interest, inasmuch as it represented the progress of a case of pancreatitis from the acute stage to the final condition resulting in complete chronic involvement of the gland. The analysis of the duodenal contents was made about seven years following the original attack, during which laparotomy was performed and drainage instituted. Six months following operation about two-thirds of the pancreas is said to have sloughed away, and there has been a fistula persisting to date. At the time of the collection of the duodenal contents the patient had an acute, severe diabetes. No enzymatic activities of the duodenal contents could be demonstrated.

The effect of pancreatic disease on the enzymatic activities of duodenal contents may be summarized from the results outlined in Table 2, as follows:

1. Extensive involvement of the pancreatic parenchyma due to acute pancreatitis, or less extensive pathology accompanying chronic pancreatitis, was associated with a decrease below the minimum normal limits of at least two of the three types of enzymatic activity in the duodenal contents. It is possible that the diminution in enzymatic activity in these cases is due, in part, to obstruction to the flow of pancreatic secretion by the pathological process, as well as to actual destruction of pancreatic parenchyma.

2. Cancer of the head of the pancreas produced a marked decrease in enzymatic activities; although extensive carcinomatous involvement of the pancreas, not involving the head or duct of Wirsung, did not demonstrably affect the enzymatic activities of duodenal contents.

3. Slight involvement of the pancreatic parenchyma, when due to acute pancreatitis, pancreatic cyst or severe diabetes mellitus did not affect the enzymatic activities of the duodenal contents.

The enzymatic activities of duodenal contents obtained from fourteen patients with va-

rious types of disease of the biliary system, including toxic and infectious jaundice, were next studied. The results are outlined in the following table. (Table 3).

Table 3

Enzymatic activities, amounts and physical character of duodenal contents obtained from patients with disease of the biliary tract, including toxic and infectious (catarrhal) jaundice.

Case No.	Enzymatic Activity			Amt in c.c.	Color	Viscosity	Diagnosis
	Proteolytic in mgm. NPN	Lipolytic in c.c. N/10 NaOH	Amylolytic in mgm. glucose				
17.x	2.9	2.8	3.1	70	white	very great	Stone in common duct, no bile excreted
18.x	2.7	1.6	0.7	100	light green	great	Stone in common duct
19.x	3.2	1.6	1.3	100	dark brown	moderate	Stone in common duct
20.	9.0	4.0	2.0	150	greenish yellow	moderate	Cholelithiasis
21.	0.8 1.6	1.8 1.0	1.4 1.3	200 75	greenish yellow	moderate moderate	Chronic hepatitis, chronic cholecystitis, diabetes
22.x	2.0 3.9	0.2 1.0	0.6 0.9	50 70	greenish yellow	moderate very great	Stone in ampulla of Vater, chronic cholecystitis, chronic hepatitis
23.	1.0 5.2	0.0 1.0	0.0 2.0	50 75	white greenish yellow	very great moderate	Stone in common duct
24.x	1.0 5.9	0.1 1.9	0.0 3.3	150 100	white greenish yellow	very great moderate	Stone in ampulla of Vater, chronic cholecystitis, chronic hepatitis
25.x	1.4	0.1	0.7	70	white	moderate	Cholelithiasis, Cholecystitis, Cholangitis
26.x	2.1	0.0	0.1	240	greenish yellow	moderate	Acute cholecystitis chronic cholesystitis, hepatitis
27.	2.2	1.0	0.8	200	greenish yellow	very great	Toxic jaundice due to arsphenamine
28.	3.1	1.0	2.5	55	white	very great	Cancer of bile ducts
29.	0.5 3.0	1.1 0.9	3.0 0.7	20 50	white golden	very great moderate	Infectious jaundice
30.	2.2	1.6	0.5	400	golden	moderate	Infectious jaundice

x = Exploratory laparotomy.

In Table 3 the enzymatic activities of duodenal contents from Cases 17, 18, 19, 20, 27 and 28 were not below the minimum normal limits, with the exception of a slight reduction in the amylolytic activity of Cases 18 and 27. At the time duodenal contents were collected all of the patients were jaundiced, except Case 26. Cases 17, 18 and 19 underwent laparotomy; Cases 20 and 28 were not operated. The preoperative diagnosis of Cases 17 and 18 was cancer of the pancreas. At laparotomy, however, no evidences of cancer were found anywhere in the upper abdominal region. The duodenal specimen for enzyme studies was obtained from Case 20 after several instillations of 33 per cent. magnesium sulphate solution, given at weekly intervals. It will be noted that in this specimen proteolytic and lipolytic activities were markedly great.

Abnormally low findings were present in duodenal contents obtained from Cases 21, 22, 23, 24, 25, 26, 29 and 30. The diagnosis given in the table represents the conditions found on laparotomy in all cases, except Cases 29 and 30.

All duodenal contents were obtained prior to operation except from Case 25.

No bile was present in the first specimens of duodenal contents obtained from Cases 23 and 24, but second specimens obtained a few days later contained much bile. In the interim between collection of the first and second specimens, Cases 23 and 24 had received duodenal lavage with magnesium sulphate solution. The first specimens of duodenal contents obtained from these cases after lavage with magnesium sulphate also contained no bile, although much bile was present in specimens taken on later dates. From such findings it is fair to conclude that obstruction to the flow of bile and pancreatic juice existed at the time of collection of the first specimens of duodenal contents. In this connection it is to be recalled that at operation Case 24 showed a stone in the ampulla of Vater.

Stones were found in the ampulla of Vater in Case 22, and a partial obstruction caused by them might explain the low enzymatic activities present in the first specimen of duodenal contents. The second specimen of duodenal contents from this case was obtained a few days later, and in the interim duodenal lavage with magnesium sulphate solution had been employed. In the second specimen the enzymatic activities were all above the lower limits of normal.

Case 25, which was explored several weeks prior to a study of the duodenal contents, showed at operation a mass of inflammatory tissue in the region of the gall-bladder, containing several gallstones. It was impossible to explore the common bile duct or the region of the pancreas. The low figures for enzymatic activity can probably best be explained by an inflammatory process involving the common bile duct, and to some extent the pancreatic duct. In Case 26 there was no jaundice, and no obstruction to the flow of bile existed at the time of operation. The low lipolytic and amylolytic activities in this case, therefore, cannot be explained as resulting from obstruction to the pancreatic duct; it will be noted that proteolytic activity was not below the minimum normal limit.

The specimens of duodenal contents obtained from Case 20 showed abnormally low proteolytic values, while the figures for lipolytic and amylolytic activity were above the minimum normal limits. These findings are not comparable to those found in the cases in which obstruction to the pancreatic duct was proved to exist, but are similar to the findings in those cases in which pancreatic disease existed (cf. Cases 12 and 14 in Table 2). Furthermore, Case 21 was not jaundiced at the time the second specimen of duodenal contents was collected. The significance of the findings will be discussed later.

The first specimen of duodenal contents was taken from Case 29 at a time when the contents obtained from the use of magnesium sulphate showed only a faint yellowish tinge. In this specimen only the proteolytic activity was below normal. A few days later the duodenal contents, following the use of magnesium sulphate, were deep golden yellow. At this time proteolytic activity was normal, while lipolytic and amylolytic values were slightly below the minimum normal limits. In Case 30 there had been almost complete absence of bile from the duodenal contents after magnesium sulphate lavage up to a few days prior to obtaining the specimen for enzyme studies. This latter specimen contained much bile, and proteolytic and lipolytic figures were normal. Amylolytic activity was much below normal. The significance of all the above findings will be discussed at the close of the paper.

The findings outlined in Table 3 may be summarized as follows:

1. Partial or apparently complete absence of bile did not in itself diminish the enzymatic activities of the duodenal contents below the minimum normal limits, when no obstruction to the pancreatic duct existed.

2. Obstruction in the ampulla of Vater was accompanied by diminished enzymatic activities of duodenal contents.

3. Diminished activity of one or more of the enzymes was found in the duodenal contents of two patients without obstruction to the pancreatic duct demonstrable at operation.

4. Toxic jaundice due to arsphenamin was not accompanied by abnormally low enzymatic activities of duodenal contents.

5. Diminished activity of one or more of the enzymes was found in the duodenal contents of two patients with infectious (catarrhal) jaundice.

Discussion. — From the standpoint of the present concepts of the physiology of digestion, as expressed in the various standard works on physiology, there are a vast number of hypothetical entities in the human intestines which can affect enzyme action. Absence of tryptic activity, for example, could theoretically be due to a lack of enterokinase, so that "trypsinogen" would not be changed into the active form, trypsin. The existence of enterokinase, however, has not been definitely proved,[5] and the same may be said of other hypothetical substances said to affect enzyme action. The great majority of these substances may have no actual existence, but may be merely the expression of certain physical chemical conditions under which enzymes act less or more efficiently. For this reason the so-called "inhibitors," "accelerators" and "activators" of enzymes will not be discussed in the interpretation of the results obtained in the work here reported. Another element of importance in interpreting the results presented in this study is the question as to inherent errors in the methods employed. The large amount of work done on normal persons and patients without pancreatic disease has satisfactorily controlled the methods and procedures, and we consider that no inherent er-

rors exist which vitiate conclusions drawn from a comparison of the results obtained in the work here presented with the findings obtained in normal individuals.

The results given in Table 1 show that normal enzymatic activities were present in duodenal contents of the patients with no detectable hydrochloric acid in the gastric contents (usual test with Toepfer's reagent). If achlorhydria gastrica existed in these patients, obviously the secretion of pancreatic juice was not dependent on the presence of hydrochloric acid injected into the duodenum from the stomach. The findings also show that pancreatic achylia did not exist, although it is frequently stated that pancreatic insufficiency is present in both achylia gastrica and pernicious anemia.

The duodenal contents of two of the patients in this series (Cases 17 and 28) apparently contained no bile. Nevertheless, the enzymatic activities were not below the minimum normal limits. In one of these patients (Case 17) laparotomy findings demonstrated no obstruction to the pancreatic duct and no disease of the head of the pancreas. In the other patient (Case 25) it seems fair to assume that neither of these conditions existed. Furthermore, the addition of human bile to duodenal contents does not increase the enzymatic activities.* From these findings it is assumed that the character of the methods used is such as to eliminate bile as a conditioning factor in enzyme activity. This conclusion is not to be construed as meaning that the action of pancreatic enzymes is not affected by the presence or absence of bile in the human intestines, but only *in vitro*, under the experimental conditions called for by the methods used in the work here reported.

The findings in Case 10, in Table 2, show that acute necrosis involving but little of the pancreas did not demonstrably affect the enzymatic activities of the duodenal contents. From this it seems reasonable to infer that the secretory activity of the pancreas was not greatly disturbed. Cases 14 and 15, on the other hand, showed greatly altered enzyme activity, and in these cases extensive destruction of pancreatic parenchyma had occurred. These findings indicate that the degree of abnormality in enzymatic activities present in duodenal contents obtained from cases of acute pancreatitis depends largely on the amount of destruction of pancreatic tissue.

Cases 14 and 15 represented acute pancreatitis. In the duodenal contents from these cases there was dissociation of enzymatic activities; *i.e.*, one or more types of enzymatic activity were of normal degree, while the remainder were below the minimum normal limits. Such findings did not occur in any of the duodenal contents obtained from a relatively large number of normal persons and patients without demonstrable pancreatic disease. For this reason the results obtained in Cases 14 and 15, in which there was extensive pancreatic disease at the time of laparotomy, are interpreted as resulting from pancreatic dysfunction.

In Cases 8 and 9 (Table 2) (cancer of head of the pancreas) the pancreatic ducts were considered to be occluded by the carcinomatous process. With one exception, the enzyme activities were considerably diminished. The exception noted occurred in the value for amylolytic action in Case 9. The activity of this enzyme may be explained either as a result of an amylase arising in the pancreas and gaining access to the duodenum through ulcerative processes, or as coming from the saliva or duodenal mucosa. In any event, the findings in these two cases indicate that in the presence of cancer of the head of the pancreas the enzyme action of the duodenal contents will be notably diminished.

The result obtained in Case 7 (cancer of body and tail of pancreas) shows that cancer of the pancreas not involving the head of that organ did not produce achylia pancreatica, although about two-thirds of the pancreatic parenchyma were destroyed.

The findings at operation in Case 11 make the diagnosis of chronic pancreatitis seem certain; and the enzymatic activities of both specimens of duodenal contents were very little.

Autopsy and histopathological findings in the case of hemochromatosis (Case 12) demonstrated that the greater part of the pancreatic tissue was anatomically intact, although there was definite sclerosis and abnormal pigment deposition. Nevertheless, the enzymatic activities of the duodenal contents were depressed much below the minimum normal limits. These findings indicate that the depression in the secretory activity of the pancreas was partly the result of a functional disturbance. Case 13 was also one of chronic pancreatitis. The clinical findings in this case show that the pancreatic parenchyma had been extensively destroyed, and it seems warranted to conclude that but little external secretory activity remained. This explains the absence of enzymatic activities from the duodenal contents. The enzymatic activities of the duodenal contents from these three cases were all very low. These findings show that the external secretory function of the pancreas was depressed.

From the above discussion it would seem justifiable to conclude that the study of enzymatic activities of duodenal contents, ascertaining the activity of the external secretory function of the pancreas, may be of distinct value: 1, in diagnosing chronic pancreatitis; 2, in locating the site of the lesion in cancer of the pancreas; 3, in estimating the amount of destruction of pancreatic parenchyma in acute necrosis of that organ.

The findings in Cases 17, 18, 19, 20 and 28 of Table 3 show, that in the presence of obstruction to that portion of the bile duct lying proximal to the pancreatic duct, and in the absence

*Unpublished observations.

of pancreatic disease, no abnormalities in the enzymatic activities of the duodenal contents were demonstrable. When obstruction to the pancreatic duct (Cases 22, 23 and 24 of Table 3) existed, enzymatic activities of the duodenal contents were much below the minimum normal level. Such results indicate that the study of duodenal enzymatic activities may furnish laboratory findings of definite value in locating a lesion causing obstructive jaundice.

Duodenal contents were taken from Case 8 (cancer of the head of the pancreas) after the employment of magnesium sulphate solution on several occasions. It will be recalled that enzymatic activities in this case were much diminished, and that the duodenal contents apparently contained no bile. In Cases 22, 23 and 24 (stone in the ampulla of Vater), on the contrary, magnesium sulphate lavage was followed by marked increase in the bile content and the degree of enzyme action in the duodenal contents. In these cases the use of magnesium sulphate lavage, combined with study of enzymatic activities, of the duodenal contents gave findings in the presence of benign obstruction which were different from those obtained when the obstruction was of malignant character. The differences were so marked as to suggest that results obtained from the combined use of duodenal lavage and enzyme concentration studies will prove to be of value in differentiating between the two types of obstruction.

In obstructive jaundice the question frequently arises as to whether the cause is benign or malignant. The three most frequent sites of malignant disease causing jaundice, are primary cancer of the head of the pancreas, primary cancer of the biliary passages, and cancer of the liver secondary to gastric carcinoma. Cancer of the stomach can almost invariably be demonstrated by x-ray examination; cancer of the bile ducts will not usually allow bile to flow into the duodenum (Case 28); and cancer of the head of the pancreas will usually occlude the pancreatic duct and largely exclude pancreatic enzymes from the duodenal contents. Thus the estimation of the enzymatic activities of the duodenal contents would seem to be of distinct value in the diagnosis of suspected cancer of the biliary tract or of the head of the pancreas.

As we stated in the body of the paper, it was not proved that a stone or inflammatory swelling of the ducts did not obstruct the pancreatic flow in Case 25. For this reason the cause for abnormal enzymatic activities found in this case cannot be definitely given. At operation it was impossible to locate the common bile duct or pancreas on account of the diffuse inflammatory process involving the entire biliary tract. In Case 26, however, the clinical findings were quite different. This patient was not jaundiced at any time and no obstructive lesions were demonstrable on laparotomy. No obstruction to the pancreatic duct was demonstrable, and the abnormal enzymatic activities present in the duodenal contents were probably the result of some other cause than parenchymatous destruction. It will be remembered that there was dissociation of enzymatic activities in this case, as well as in Cases 21, 29 and 30. These findings are comparable to those occurring in acute pancreatic necrosis (Cases 14 and 15) in which there was undoubtedly derangement of the external secretory function of the pancreas. For this reason it is considered probable that similar derangement existed in Cases 21, 26, 29 and 30, but until further experimental evidence is available, an exact interpretation of these anomalies cannot be made.

The results obtained in studying Case 15 (acute pancreatitis) suggests definitely that periodic estimations of enzymatic activities in the duodenal contents furnish a rational method of following the progress of cases of pancreatic insufficiency.

The question arises as to the need for the rather complicated and time-consuming processes of obtaining duodenal contents and of estimating their enzymatic activities. It has been urged that any secretory anomalies of the pancreas would be reflected in the stools, and that the examination of the stools would suffice. That such is not necessarily the case is evident from the findings in Case 11 (chronic pancreatis) in which careful stool examinations were made on successive days following a Schmidt test diet.

All the examinations were negative. In several of the other cases here reported the stool examinations on house diet showed no evidences of abnormal digestion. In cases with a low sugar tolerance, furthermore, it is obviously inadvisable to feed proper test diets for satisfactory stool examination. Also, examination of stools will be of no aid in the diagnosis of pancreatic disease when bile is excluded from the intestines or when pathological conditions prevent the absorption of food from the small intestines. In addition, it is well known that bacteria always present in human intestines can duplicate all phases of enzyme digestion, so that it is conceivable that bacterial action alone could mask evidences of pancreatic disease as obtained from stool examination. In this connection it is of interest to note that McClure, Vincent and Pratt[6] found that completely depancreatized dogs could often utilize a considerable percentage of protein and fat of food ingested. It seems clear, therefore, that pancreatic disease may not be evidenced by stool findings alone. In selected cases, therefore, the use of the methods described and used in this work will be found of aid in diagnosis and in following the progress of a given case.

CONCLUSIONS.

1. Abnormalities in enzymatic activities of duodenal contents, demonstrated by the methods and procedures used in the work here reported, were found: (a) in the presence of some organic lesion involving the pancreas primarily or sec-

ondarily; or (b) when clinical, operative or autopsy findings indicated the possibility of derangement of the external secretory function of the pancreas. It seems fair to assume, therefore, that such abnormalities show pathological involvement of the pancreas or its ducts, and that the involvement of the pancreas may be mechanical or functional in nature. If this assumption is correct, then it is justifiable to conclude that estimation of enzymatic activities of duodenal contents furnishes an index to the activity of the external secretory function of the pancreas.

2. In achylia gastrica and pernicious anemia no abnormalities in the activity of the external secretory function of the pancreas were demonstrable, as measured by the enzyme concentration of duodenal contents. These findings suggest that the presence of hydrochloric acid is not necessary in order to stimulate normal pancreatic secretory activity.

3. Under the experimental conditions used, enzymatic activity was not demonstrably affected by the presence or apparent absence of bile in the duodenal contents.

4. The external secretory function of the pancreas, as measured by the enzyme concentration of duodenal contents, was found to be much depressed in chronic pancreatitis.

5. Acute pancreatic necrosis, cancer of the head of the pancreas and lesions obstructing the pancreatic duct were accompanied by marked abnormalities in enzymatic activities of duodenal contents. Obstructive lesions caused great diminution, while acute necrosis usually caused dissociation in enzymatic activities.

6. Estimation of enzymatic activities of duodenal contents furnished findings of value in the differential diagnosis between benign and malignant lesions, causing obstructive jaundice.

7. Dissociation of enzymatic activities of duodenal contents are interpreted as showing derangement of the external secretory function of the pancreas.

8. Acute and chronic cholecystitis and infectious (catarrhal) jaundice were accompanied by dissociation of enzymatic activities of duodenal contents. This finding suggests that there was associated derangement of the external secretory function of the pancreas.

CASE REPORTS OF IMPORTANCE IN AIDING THE READER IN THE INTERPRETATION OF THE EXPERIMENTAL RESULTS HERE REPORTED ARE APPENDED.

CASE No. 7.—A. T., male, aged 48. E. S. 248869.

Admitted to Massachusetts General Hospital March 31, 1922, and discharged April 29, 1922.

Diagnosis: Carcinoma of pancreas (not involving the head). Diabetes mellitus (mild).

At operation the tail and body of the pancreas were found to be largely invaded by carcinoma. However, the head of the pancreas was not involved and there was no demonstrable obstruction to either the pancreatic or bile ducts.

CASE No. 8.—W. E. H., male, aged 49. Med. No. 14946.

Admitted to Peter Bent Brigham Hospital December 7, 1921, and discharged December 31, 1921.

Diagnosis: Cancer of head of the pancreas.

Patient was a man 49 years of age, whose past medical history is essentially negative. During the past 18 months prior to admission to the hospital the patient had been troubled with malaise, lassitude and physical weakness. Jaundice had been present seven months. Onset had been painless and associated with dyspepsia, diarrhoea and excessive thirst. On physical examination the patient showed deep icterus and was much emaciated. The liver was markedly enlarged, the left lobe measuring 1.5 cm. below the costal margin in the midclavicular line. The surface of the liver was smooth and the edge firm. In the right upper quadrant, below the liver edge, a smooth, firm mass about the size of a lemon was palpable.

X-ray studies showed no abnormalities in the gastrointestinal tract.

Clinical examination of the blood showed a moderate degree of secondary anemia. Gastric analysis showed normal acidity. The urine and stools were those usually found in obstructive jaundice. Operation was refused.

CASE No. 9.—J. E. T., male, negro, aged 56. Med. No. 19653.

Admitted to Peter Bent Brigham Hospital May 22, 1922, and transferred to Surgical Service May 30, 1922.

Diagnosis: Carcinoma of head of pancreas (involving the common bile duct).

Past Medical History was essentially negative.

The present illness began six weeks prior to admission to the hospital. During the first two weeks there were gaseous bloating of the epigastrium and epigastric distress at night; relieved by soda or hot water. The taking of food caused dull aching in the epigastrium, beginning five to ten minutes after eating and lasting from three to twelve hours. Jaundice developed four weeks prior to admission to the hospital, and was accompanied by pruritus and profuse sweats. Lying on the right side caused nausea. Slight dyspnoea had been present since the onset.

On physical examination the sclerae and skin were deeply jaundiced. The liver edge was palpable 5 cm. below the right costal margin; it was firm and irregular. There was moderate tenderness in the epigastrium, more particularly just to the right of the midline. There was right inguinal hernia. Otherwise the physical examination was negative.

Fluroscopic examination demonstrated a concave defect in the outline of the lesser curvature

side of the antrum and first portion of the duodenum. This finding suggested pressure from without.

Hemoglobin was 88 per cent., white blood cells 9,000 and red cells 4,000,000 per c.mm. The smear was not unusual. Wassermann reaction was negative. Gastric analysis showed a moderately low free HCl and total acidity. Benzidin test was negative. The findings in the urine and stools were those usual in obstructive jaundice. At operation a large adenocarcinoma of the head of the pancreas, involving the common bile duct, was found.

CASE No. 10.—E. S. R., male, aged 40. W. S. 248407.

Admitted to Massachusetts General Hospital March 8, 1922, and discharged April 29, 1922.

Diagnosis: Acute pancreatitis. Chronic cholecystitis. Cholelithiasis.

The patient entered the hospital complaining of attacks of epigastric pain, vomiting and jaundice and of constipation. The past history was essentially negative.

During the past four years prior to admission to the hospital the patient had had attacks of severe epigastric pain, lasting about seven to twenty-four hours and accompanied by repeated vomiting of foul, greenish material, and by constipation. Such attacks occurred at intervals of four or five months. In one attack jaundice had occurred. The present attack had developed ten days before admission. The pain was paroxysmal in character, sharp in nature and located in mid-epigastrium. The bowels were constipated.

On physical examination moderate tenderness and muscular rigidity were found in the left upper abdominal quadrant, in the region of the gall-bladder. The patient was definitely jaundiced. X-ray of gall-bladder region showed shadows suggesting biliary calculi.

Laboratory findings: Hemoglobin was 85 per cent. and white cells 10,000 per c.mm. The Wassermann was negative. The findings of the stomach contents after an Ewald breakfast were normal. The stools were not abnormal and contained bile.

March 14. Operative note: The gall-bladder wall was thickened and showed an area of fat necrosis (also demonstrated microscopically in sections). The gall-bladder contained two stones and much dark fluid. The pancreas was found to contain areas of necrosis and the gastro-colic omentum showed areas of fat necrosis.

CASE 11.—F. H., male, aged 50. E. S. 250706.

Admitted to Massachusetts General Hospital July 9, 1922.

Diagnosis: Chronic cholecystitis. Cholelithiasis. Chronic pancreatitis.

Patient entered the hospital complaining of epigastric pain and loss of weight.

The past history was essentially negative. Venereal infection was denied.

Present Illness: For the last six months the patient had suffered from attacks of epigastric pain, non-radiating, coming on at intervals of several days to weeks, with no apparent relation to meals. Pain was not severe until recently, did not cause vomiting, and was not severe enough to make the patient cry out. It never waked the patient up. It was relieved at first by walking about, but recently not relieved by ordinary procedures. There had been no jaundice, hematemesis, melena, urinary abnormalities.

During the last few weeks prior to admission, attacks have occurred several times daily, and have lasted from half an hour to several hours. There was no diarrhea or constipation. During the last six months the patient had lost about thirty pounds in weight.

Physical Examination: Well developed somewhat emaciated man. Skin very dark, where it had been exposed to sun and heat, but no abnormal areas of pigmentation. In the mid-epigastrium there was an indefinite mass, which was tender, not movable, pulsating but not expansile. In the right upper quadrant there was increased muscular resistance, but no definite mass was palpable.

Laboratory Findings: Blood and urine were essentially negative. The blood Wassermann was negative. Examination of the stools following a full Schmidt test diet was absolutely negative. X-ray examination of the gastrointestinal tract failed to show any abnormal findings, except that the stomach seemed to be pushed somewhat forward as if a mass was behind it. Barium enema was negative.

Operation: At operation a large, thickened gall-bladder was found, with a single stone in the cystic duct. The pancreas was enlarged and extremely hard throughout, and on palpation it seemed typical of advanced interstitial pancreatitis.

CASE 12.—J. E. O'M. Male, aged 43. E. M. 248570.

Admitted to the Massachusetts General Hospital March 15, 1922, and died April 4, 1922.

Diagnosis: Hemochromatosis. Chronic pancreatitis. Syphilis. Diabetes mellitus. Hypertrophic cirrhosis of the liver. Acute colitis. Bronchopneumonia.

Patient entered the hospital complaining of epigastric pain, dizziness, faintness, weakness and cough.

The patient has been a moderate user of alcohol. At the age of 18 he had pneumonia. Eighteen years prior to admission he had a bubo in the left groin. Nine years prior to admission a hard chancre developed on the penis, but no antiluetic treatment had been taken. No secondary eruption had been observed. Eight years ago there had been an attack of acute

arthritis, and, during the same year, an attack of malaria.

Present Illness: For ten years there had been vague, indefinite epigastric "pain" about 30 minutes after dinner and supper, lasting five to ten minutes. The "pain" radiated to the left axillary region and to the back. The "pain" occurred three or four times a week and was associated with nausea, occasional vomiting, and always with dizziness, faintness and weakness. During the two weeks prior to admission the epigastric pain had disappeared. For two months prior to admission the patient had an excessive appetite, marked thirst, polyuria and loss in body weight from 158 to 124 pounds. Two years prior to admission his family physician discovered glycosuria. In December, 1921, the patient had fractured a rib. Since then there had been a distressing cough which was unproductive until a week before admission. During this time sputum was raised. There had been no hemoptysis, but during the two weeks prior to admission night sweats had occurred.

Physical Examination: Emaciated. Skin dark, but no definite areas of pigmentation. Liver definitely enlarged, edge smooth.

Laboratory Findings: The hemoglobin was 70 per cent. White blood cells were 8000 per c.mm. Blood sugar was 0.3 per cent. on admission, but dropped to 0.1 per cent. on starvation. The blood Wassermann was positive.

On admission the 24-hour output of urine was between 3000 and 4000 c.c., and contained about 7 per cent. glucose. Under treatment the 24-hour amount dropped to 1000 to 1500 c.c. and the glucose to 1 to 2 per cent. With onset of fever, acetone and diacetic acid appeared in the urine. All stools examined were the result of enemata. These stools contained much pus and mucus.

During his stay in the hospital diarrhoea developed, and later bronchopneumonia, of which the patient died. Duodenal specimen was obtained on the day before onset of diarrhoea, and before the patient's condition became dangerous.

Autopsy Findings were typical of hemochromatosis, with marked pigmentation and fibrosis of the liver and pancreas.

Case 13.—D. C. White, male, aged 54. E. M. 205738.

Admitted to Massachusetts General Hospital June 10, 1922.

Diagnosis: Chronic pancreatitis. Diabetes mellitus. The past history was essentially negative.

During the year 1915 the patient had had dull epigastric pain, coming on two or three times a week and occurring 30 minutes after the midday meal. The pain was relieved by hot water. At the end of this year, one morning, just after breakfast, the patient was seized suddenly with severe, colicky epigastric pain, requiring morphine for its relief. This pain radiated around both hypochondriac regions to the back. It persisted for several days. The patient was then admitted to the Massachusetts General Hospital. On admission physical examination showed epigastric tenderness and spasm. The liver edge was palpable 2 cm. below the right costal margin. In the right hypochondrium a round, smooth, tender mass was palpable. The diagnosis of subacute perforation of the stomach was made. At operation acute pancreatic necrosis was found to be the cause of the trouble. The gall-bladder was normal.

Six months after the operation a large slough of degenerated pancreatic tissue was discharged through the fistula which had persisted after laparotomy. Since the time of operation up to the present date (June 15, 1922) the fistula has remained open. Since that time the patient had few subjective symptoms, except when full drainage from the fistula was interrupted. A few weeks prior to the present examination he was told there was sugar in his urine.

On admission, June 10, 1922, the patient complained of no subjective symptoms. The physical examination showed the fistula, and the liver edge was palpable 2 cm. below the right costal margin. The patient was 25 pounds under weight.

The usual clinical examinations of the blood were negative. Blood sugar was 0.2 per cent. Sugar tolerance test showed extremely high figures. The urine was negative (patient sugar-free on diet). The stools showed an excess of fat. The duodenal contents contained an excess of bile pigments, but showed no enzyme action.

Case 14.—I. G. Female, aged 38. W. S. 247759. Admitted to the Massachusetts General Hospital February 1, 1922, and discharged April 5, 1922.

Diagnosis: Acute hemorrhagic pancreatitis. Acute cholecystitis.

Past medical history essentially negative.

Present Illness began three days prior to admission to the hospital, with sudden, moderately severe, colicky pain in the dorso-lumbar region, which soon spread over the entire abdomen. This pain was present on admission to the hospital. Although nausea had been constantly present, vomiting had occurred but once. There was anorexia and the bowels were obstinately constipated.

On physical examination the patient appeared to be in moderate discomfort. The abdomen was diffusely tender and spastic, especially in the midepigastrium. The temperature was 102, the pulse 110, and the respiration 24.

The blood count showed 10,000 white cells per c.mm. The Wassermann was negative. The urine was negative. Stools resulting from enemata were very light brown in color and con-

tained microscopically increased amounts of fat droplets and fatty acid crystals. At the time of the first examination of duodenal contents for enzymatic activities (two weeks after operation) the stools were normal.

Operative note, February 1, 1922: Considerable free fluid in abdomen, at first straw colored and then blood tinged. Spots of fat necrosis were everywhere seen and were most numerous in the gastro-colic omentum near the pyloric end. The pancreas was inflamed and showed three hemorrhagic areas and an area of fat necrosis 5 cm. in diameter. The gall-bladder was small and its walls thickened, and it contained bile and purulent material.

CASE 15.—J. F. M. Male, aged 30. W. I. 248024. Admitted to the Massachusetts General Hospital February 15, 1922, and discharged March 9, 1922.

Diagnosis: Acute hemorrhagic pancreatitis.

Since the age of 14 the patient had taken a cathartic daily for constipation; also, during this period there had been recurring attacks of obstipation, associated with abdominal distention and discomfort. During the three months previous to admission the patient had gained 24 pounds in weight, the abdomen had gradually enlarged, and dyspnoea on strenuous exertion had developed.

Present Illness: For the past week before admission to the hospital the patient had been more constipated than usual, with some abdominal distress. Two days ago he developed great discomfort in the abdomen, described as a marked sensation of pressure over the entire abdomen. The night before admission this feeling was so pronounced that he "thought he would die." There had been no colicky pains. He had been well morphinized by his physician. During the past two days there had been frequent vomiting, and not even water was retained; there had been no fecal vomiting. The bowels had not moved, but an enema on morning of day of admission produced a moderate result and flatus was passed that same evening. On the night of admission the patient felt comfortable.

On physical examination the patient appeared to be but slightly ill. Shifting dulness was demonstrable in the flanks, but no other abnormalities were noted in the abdomen. Temperature was 100.6, pulse 110, and respiration 22.

Hemoglobin was 80 per cent. White cells were 22,300 per c.mm., with 90 per cent. polynuclears. The Wassermann reaction was negative. The vomitus was dark green in color and strongly acid. Stools examined on February 24, 26, 28 and March 2 showed an excess of fat, but were not pasty in appearance. The urine showed a slight trace of albumin, and for the first few days after admission a slight trace of sugar.

Operation, February 16, 1922. The abdominal cavity contained blood-tinged fluid. The mesentery and omentum were spotted with areas of fat necrosis. The pancreas "had a soft necrotic feeling."

Patient was discharged to Out-Patient Department, March 9. Sugar tolerance test showed normal findings two weeks after the third specimen of duodenal contents was obtained for enzyme studies.

Duodenal contents were examined on March 7, 30, April 13 and July 17. When last seen the patient was in fairly good condition, and was gaining weight and strength.

CASE 17.—A. J. McC. *Preoperative Diagnosis:* Cancer of the head of the pancreas.

Postoperative Diagnosis: Chronic cholecystitis. Cholelithiasis; stone in common bile duct.

April 9, 1921. Patient was a housewife, 61 years of age. She had been jaundiced for one week, one and a half years ago. Fourteen months ago the left breast had been removed because of a nonmalignant growth about 10 cm. in diameter. Patient had first noticed jaundice four weeks before admission, associated with anorexia, nausea, epigastric distress and some loss in weight. On physical examination the patient showed deep jaundice; the liver edge was indefinitely felt 2 cm. below costal margin and the ascending colon was palpable.

Roentgen examination showed gastric hyperperistalsis and the second portion of the duodenum was moderately dilated.

From April 9th to 29th the jaundice remained unchanged. During that period the patient vomited all food taken up to April 22nd, after which date vomiting was less pronounced. The liver edge became palpable 4 cm. below the costal border. There developed a small, firm, nontender, egg-shaped mass, just below the edge of the liver in the midclavicular line.

Laboratory findings were essentially negative except for bile in the urine and fatty stools usual in obstructive jaundice.

On laparotomy, a large calculus was found in the ampulla of Vater. There was, however, no distention of the common bile duct, which did not contain bile. The gall-bladder was greatly distended, but the contained fluid was not bile colored.

May 13, 1922. The patient recovered and has been in good health to date.

CASE 18.—F. H. W. White female, aged 59. Med. No. 133791. Admitted to Massachusetts Homeopathic Hospital Nov. 26, 1921 and died Dec. 10, 1921.

Preoperative Diagnosis: Cancer of the head of the pancreas. *Postoperative Diagnosis:* Chronic cholecystitis, cholelithiasis.

The past medical history was essentially negative.

The present illness had begun four weeks prior to admission to the hospital. The earliest symptoms had been those of moderately severe dyspepsia, followed in a few days with jaundice

of the skin and sclerae. There had been no abdominal pain.

On physical examination the patient was seen to be deeply jaundiced. Her mentality was considerably dulled. The liver edge was palpable 3 cm. below the right costal margin. Its edge was rounded and its surface smooth.

The usual clinical examinations of the blood, including the Wassermann reaction, were negative. The urine and stools were those usual in obstructive jaundice.

At laporotomy a stone obstructing the common duct and located proximal to the ampulla of Vater was found.

CASE 21.—A. C. Italian male, aged 58. E. M. 249521. Admitted to Massachusetts General Hospital May 5, 1922, and discharged June 1, 1922.

Diagnosis: Chronic hepatitis. Chronic cholecystitis. Diabetes mellitus.

Past medical history was essentially negative.

Sixteen, fourteen, thirteen and twelve years prior to admission to the Massachusetts General Hospital the patient had had attacks of severe epigastric pain, associated with jaundice. Thirteen years prior to admission the gall-bladder region had been explored at laparotomy. Many adhesions were found about the gall-bladder, but no gallstones. The present attack was similar to those occurring in the past; and together with those occurring in the past was associated with a moderate degree of diarrhoea. During the three months prior to admission there had been polyuria and polydypsia; glycosuria had been demonstrated recently in the Out Patient Department of the Hospital.

On physical examination at the time of admission the patient's sclerae were jaundiced and he was considerably under weight. The edge of the liver was palpable at the right costal margin, while the spleen reached 4 cm. below the left costal margin.

Hemoglobin was 65 per cent., white blood cells 6,500 and red cells 5,544,000 per c.mm. Blood sugar was 0.2 per cent. The urine showed no bile; the stools did not show abnormal amounts of fat.

On May 10th, 1922, duodenal contents collected for enzyme studies contained much bile. At this time 60 c.c. of 33 per cent. magnesium sulphate were instilled into the duodenum. Duodenal contents were again collected on May 15, and contained much bile. At the time of the second collection the patient was not jaundiced, although the blood plasma contained an excess of bile pigment.

CASE 22.—M. N. Female, aged 52. W. S. 248135. Admitted to Massachusetts General Hospital February 21, 1922, and discharged April 5, 1922.

Diagnosis: Cholelithiasis. Chronic cholecystitis.

Complaint: Epigastric pain and jaundice of four months' duration.

Past medical history was essentially negative.

Present illness. Fourteen years prior to admission the patient had been "yellow sick" for six weeks. The present illness began four months before admission. During this period there had been attacks of severe pain, beginning in the right upper abdominal quadrant and radiating around the left costal margin to the dorso-lumbar region of the back. With the onset jaundice had developed and still persisted on admission to the hospital, although it had varied in its intensity. Anorexia was present and the patient had lost 17 pounds in weight.

On physical examination jaundice of the skin and sclerae was noted. Otherwise the physical examination was essentially negative.

X-ray studies of the gastro-intestinal tract were negative.

Hemoglobin was 80 per cent. and white blood cells 10,000 per c.mm. The Wassermann on the blood serum was negative.

Gastric analysis showed no free HCl and total acidity of 14. On February 26 the bile pigment in the duodenal contents was about one-third the normal amount and enzymatic activities were low. On February 28, the pancreatic enzyme action was normal. A solution of 33 per cent. magnesium sulphate had been instilled into the duodenum following the first examination.

Operation March 7, 1922. Gallstones were removed from the common duct, which was dilated. The gall-bladder was thickened and bound down by adhesions.

CASE 23.—A. J. B. Med. No. 17493. Admitted to Peter Bent Brigham Hospital December 31, 1921, and discharged January 23, 1922.

Diagnosis: Gallstones. Questionable syphilis.

Patient is a well-developed Hebrew of 47, who gives a definite history of syphilis, including primary and secondaries of 18 years ago, and also of central nervous system lues ten years ago. Adequate treatment had been taken; and on admission to the hospital the Wassermann on the blood serum was negative. Fourteen years ago the patient had been jaundiced for four days. The present attack of jaundice began six weeks prior to admission to the hospital and had progressively deepened. Associated symptoms were nausea one hour after meals and girdle pains of greatest intensity in the dorso-lumbar region, radiating to the shoulder blades.

On physical examination icterus was deep. The liver edge was 5 cm. below the costal border. The liver surface was smooth and the edge soft.

Roentgen examination showed the duodenum to be persistently flattened on its superior surface, and on this surface its outline was half-moon shaped. This finding suggested an extra-duodenal lesion. The large bowel was not unusual by barium enema.

The usual laboratory examinations of the blood and gastric contents were negative. The

urine and stools showed the findings usual in jaundice. Wassermann reaction on blood serum was negative.

Duodenal lavage, 33⅓ $MgSO_4$, 50 c.c., on January 4 and 5; 400 c.c. and 320 c.c. of colorless fluid obtained. January 11, after a meal of 40 c.c. of 20% cream mixed with 10 gms. $BaSO_4$ the duodenal contents were light yellow in color (due to bile).

January 23, discharged; less jaundiced than on admission and in good general condition.

CASE 24.—M. W. Female, aged 53. W. S. 247363. Admitted to the Massachusetts General Hospital, January 12, 1922, and discharged February 11, 1922.

Diagnosis: Cholelithiasis. Chronic cholecystitis.

The past medical history was essentially negative.

Present Illness: Two years before admission to the hospital there had been an attack characterized by dull epigastric pain, some vomiting and much weakness. This attack lasted one week. Eight months before admission the patient had been studied on the Surgical Service of the Peter Bent Brigham Hospital. At that time she had been jaundiced for six weeks and complained of much dull pain in the right side of the epigastrium. The jaundice remained for nearly three months and then gradually disappeared. During the next five months the patient was free from symptoms, except for transitory, mild epigastric pain. The patient then became jaundiced again and entered the Massachusetts General Hospital.

Physical examination showed the patient to be somewhat emaciated. The skin and sclerae were jaundiced. The liver edge was palpable 3 cm. below the right costal border.

Hemoglobin was 75 per cent. and white blood cells 11,200 per c.mm. The urine contained very little bile and occasionally some sugar. The stools were light brown in color and microscopically showed large amounts of fatty acids (patient on a low fat diet). The duodenal contents contained much bile after the use of magnesium sulphate.

At operation the gall-bladder contained many stones and a stone was found in ampulla of Vater. The gall-bladder and bile ducts were markedly thickened, and the pancreas was hard and apparently fibrosed.

CASE 25.—N. M. Female, aged 53. W. S. 248020. Admitted to the Massachusetts General Hospital February 15, 1922, and discharged April 13, 1922.

Diagnosis: Cholelithiasis. Chronic cholecystitis. Chronic cholangitis.

Complaint: Attacks of pain under right costal margin, of seven to eight months duration.

Past medical history was essentially negative.

Present Illness: During the seven or eight months previous to admission there had been attacks of pain in the gall-bladder region. The pain was severe at times and radiated to the interscapular region of the back. The attacks usually occurred at night and lasted several hours. At times the stools had been white and the urine very dark in color. The right upper quadrant of the abdomen had been tender. For the past week the bowels had been constipated.

On physical examination icterus of the skin and sclerae was present. The patient was totally deaf. A mass about 3 cm. in diameter was palpable in the right epigastrium, with associated spasm and tenderness.

Hemoglobin was 95%. White blood cells were 18,800 per c.mm., with 82 per cent. polynuclears. The urine and stools were of the character usually found in obstructive jaundice.

Duodenal tube introduced on March 16th. After instillation of 50 c.c. of 33 per cent. magnesium sulphate the fluid obtained was colorless. Following this the cream meal was given and duodenal contents obtained for enzymatic studies.

Operation, February 23, 1922. The gall-bladder was imbedded in a mass of inflammatory tissue and was packed with gallstones. It was impossible to explore the common bile duct or region of the pancreas on account of the extent of the inflammatory process.

The patient was discharged nearly two months after the operation. During this time complete obstruction to the flow of bile into the duodenum remained and the jaundice was unchanged.

CASE 26.—A. F. Male, aged 61. W. S. 428283. Admitted to Massachusetts General Hospital March 1, 1922, and died March 9, 1922.

Diagnosis: Acute cholecystitis. Pylephlebitis.

Six years prior to admission the patient was sent to Westboro because of "nervous breakdown." During the past five years there had been occasional attacks of dyspepsia characterized by "sour stomach," belching and epigastric distress after meals.

Present Illness: Six days ago while at work patient was seized with a sharp, knife-like pain below the ensiform, rather spasmodic, but persisting without definite remission until the present. He was able to finish his day's work, but went to bed that evening and stayed there. The pain became duller, spread downwards and backwards over the abdomen and into the flanks and was fairly constant. It was made worse by exertion and was not affected by vomiting or by movements of the bowels. He vomited twice that day, and vomited practically everything eaten since then, but never blood. The vomitus always tasted very sour. He obtained several loose movements a day by the use of salts. He felt feverish several times and sweat a great deal. His urine had been scanty and high colored.

On physical examination the skin was flushed

and moist. There was some dyspnea, although no cardiac lesion was demonstrable. Percussion demonstrated shifting dulness in the flanks. There was moderate tenderness along the right costal margin and in the mid-epigastrium.

The white blood count was 14,000 and 15,000 per c.mm. Wassermann was negative. Urine and stools were negative. On March 7 the duodenal contents contained a large excess of bile pigments and the sediment indicated inflammation of the entire biliary tract.

Operation, March 9, 1922. Distended and thickened gall-bladder, without stones, was found. It contained dark, tarry bile and was evidently infected.

Case 28.—D. B. Male, aged 50. W. M. 247541. Admitted to Massachusetts General Hospital January 20, 1922.

Diagnosis: Obstructive jaundice. Carcinoma of the gall-bladder, bile ducts and liver.

Past medical history was essentially negative.

Present Illness: Eight weeks before admission patient had an upper respiratory infection, followed one week later by jaundice. The jaundice did not clear up under treatment, and after five weeks' severe pruritus became an additional symptom. He went to a hospital, but showed no improvement after three weeks' care. On admission to the Massachusetts General Hospital the presenting symptoms were deep jaundice, pruritus, anorexia, fatigue and insomnia. There had been no abdominal pain at any time. Urine had been dark and stools clay colored since onset. There had been no fever or chills. About thirty-five pounds had been lost in two months.

Physical examination showed a well-developed, somewhat emaciated man, deeply jaundiced. The skin was deep greenish yellow and showed many abrasions from scratching. Liver dulness reached up to the 4th interspace and the liver edge was felt 1 cm. below the right costal margin. In the left epigastrium a small, round, movable mass was felt just under liver edge, moving with respiration; this was probably the gall-bladder.

X-ray studies of the gall-bladder and gastro-intestinal tract were negative.

Red blood cells were 3,984,000 per c.mm. and white cells 10,000 to 14,000 per c.mm. The differential count was normal. The Wassermann reaction on the blood serum was negative. The gastric analysis showed free HCl 29 and total acidity 60. Duodenal contents showed no bile after food or after the instillation of magnesium sulphate into the duodenum. The urine and stools were of the character usual in obstructive jaundice. Operation was refused.

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CONGENITAL OBLITERATION OF THE BILE DUCTS AND CONGENITAL BILIARY CIRRHOSIS OF THE LIVER.*

BY J. KEITH GORDON, M.D., BOSTON.

The incidence of cases reported in the literature as congenital biliary cirrhosis of the liver *per se* is a comparatively low one. In most instances the condition has been associated with an obliteration of the main bile passages, with the result that the cirrhotic feature itself has been regarded as a secondary and perhaps less important process.

In 1911 Howard and Wolbach[2] reviewed the literature and succeeded in collecting seventy-six cases of congenital obliteration of the bile ducts, including a case of their own, and exclusive of those directly associated with syphilis. With the exception of nine of the earlier cases, a microscopical examination of the tissues had been a routine procedure and the constant accompanying finding had been a cirrhosis of the liver, the biliary type predominating. They divided the cases they encountered into the following groups:

I. Obstruction of the hepatic and common ducts; gall-bladder and cystic duct patent.

II. Obliteration of the gall-bladder and cystic duct; hepatic and common ducts patent.

III. Obliteration of the cystic and hepatic ducts; common duct patent.

IV. Obliteration at a variable point below the junction of the cystic and hepatic ducts.

The majority of these cases fell into Group III.

J. B. Holmes[3] in 1916 reported a case and made an exhaustive review of the literature on the subject. In addition to his own he cited 108 authentic cases of congenital obliteration of the bile ducts and by means of eighty excellent drawings representing the conditions as he found them showed diagrammatically at what point or points in the extra-hepatic biliary apparatus there might be an anatomical cause for interference with function. In reality these diagrams but represent in detail the broad classification of Howard and Wolbach with the addition of two conditions evidently overlooked by the latter writers, namely, the obliteration of the extra-hepatic biliary apparatus in its entirety, and a complete absence of any part or parts thereof. Holmes' lucid and concise diagrams are of particular interest to the surgeon, to whom he thus demonstrates how operative

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procedures in effecting a passage of bile to the duodenum would be possible in a fair percentage of cases.

In a series of 1086 consecutive autopsies at the Children's and Infants' Hospitals, Boston, there have occurred but four cases of congenital obliteration of the bile ducts. Briefly, the case histories and pathological findings of these cases are as follows:

Baby H. P., female, aged 5 months, was admitted to the Infants' Hospital on July 30, 1915, with the following history: The father and mother were living and well. There was one other child living and well. There were no deaths, stillbirths, miscarriages, or history of tuberculosis in the family. The patient was a full-term baby with normal delivery, and had always been breast-fed. He vomited constantly since birth. There had been no jaundice during the first two weeks, since which time jaundice had developed and had been progressive. Coincident with this the stools had been clay-colored and the urine dark. The baby had lost weight during the month prior to admission.

Examination of the patient revealed nothing abnormal except a generalized icterus with clay-colored stools and highly colored urine. Seven days after admission the liver and spleen became palpable. Bronchopneumonia developed and the child died on the 10th day after admission. An autopsy was performed thirteen hours after death and the following are the main features abstracted from the protocol: General icterus was present. The liver weighed 320 grams and was firm in consistency. Its surface was very irregular, having a fine hob-nailed appearance. The color of the peritoneal surface was a dark greenish purple. The cut surface showed a fine hob-nailed appearance similar to that seen on the peritoneal surface. Between the liver lobules there was a fibrosis which in the gross appeared as fine white lines. The gall-bladder had no cavity and presented as a mass of fibrous tissue. The hepatic, cystic, and common ducts were all obliterated, forming fibrous cords without any lumen. The papilla of Vater was not visible.

The spleen weighed 70 grams. There were patches of consolidation in both lungs.

Microscopically the liver showed a fibrous connective tissue increase, confined practically to the portal areas and about the lobules. The connective tissue did not extend extensively into the lobules, nor was it increased around the central veins. The bile ducts in the portal spaces were increased in number, but not dilated. Some of the larger ones contained bile casts. The capillaries also were increased in number. In some areas there was a rather extensive vacuolization of the liver cells.

Thus, in recapitulation, a female infant developed jaundice two weeks after birth. She was admitted to hospital at the age of five months, was deeply jaundiced, and died ten days after admission. An autopsy revealed complete obliteration of the gall-bladder, and cystic, hepatic and common ducts. Microscopically the liver showed a biliary cirrhosis.

A case of this kind might constitute a possible Group V.

A second case, reported by Dunn[3] in 1916, showed no gall-bladder or extra-hepatic duct pathology, but microscopically the liver gave evidence of a mixed type of cirrhosis, together with an extreme degree of degeneration of the liver cells.

This might constitute a seventh group.

A third case is as follows:

Baby F. B., female, aged 7 days, was admitted to the Infants' Hospital on May 10, 1919. The following history was obtained from the parents: The father, mother, and one other child were alive and well. There was no history of miscarriages. In April of the previous year a child had been born which became markedly jaundiced on the second day after birth and died three days later. The patient was a full-term baby, apparently normal at birth, but became jaundiced on the second day. The jaundice increased each day. The stools were white, and the urine highly colored. On examination the liver was palpated 3 cm. below the costal border and the spleen was also palpable. Except for a deep icteroid tinge to the skin, sclerae, and buccal mucosa, there were no abnormal physical signs. The child died soon after admission to hospital. An autopsy was performed, and the following are the main features abstracted from the protocol:

There was generalized icterus. The liver extended 3 c.m. below the right costal border and 3 c.m. below the ensiform. It weighed 175 grams and was moderately enlarged. Its surface was smooth and of a dusky red color. On section the lobular markings were indistinct and the cut surface had a yellowish cast to it. The hepatic veins contained fluid blood. The gall-bladder was narrow and shrunken, though containing about 2 c.c. of black mucilaginous bile. It was possible to pass a probe through the cystic duct in its entire length. The hepatic duct had a lumen too narrow for the smallest probe available. The common duct was represented by a narrow fibrous cord in which no lumen could be demonstrated either by expression of bile, passage of probe, or dissection. The other organs were not remarkable in the gross.

Microscopically the normal architecture of the liver was preserved, but there was moderate congestion and oedema separating the columns. There were acute degenerative changes in the liver cells in the mid and peripheral zones, with necrosis and invasion by many polymorphonuclear leucocytes. Inspissation of black bile in

the bile capillaries was prominent. Bile had also escaped from the bile capillaries and lodged outside the liver cells, where it was taken up in quantity by endothelial phagocytes. There was a slight increase in fibrous tissue about the portal areas, and this was infiltrated with lymphoid cells, eosinophiles, and a variable number of polymorphonuclears. The bile ducts were not dilated. Many contained plugs of brownish black bile and were lined by rather low epithelium. A few showed proliferation. There was no fat in the liver cells.

To sum up: a female infant developed jaundice on the day of birth. This condition increased until death occurred on the seventh day. On autopsy an obliteration of the common duct was found. The hepatic, cystic ducts and gall-bladder were patent. Microscopically the liver showed focal necroses and a mild type of biliary cirrhosis. The case corresponds with Group IV, according to Howard and Wolbach's classification.

The case history and pathological findings of a fourth case, which corresponds very closely to that of Dunn's, are as follows:

Baby S. W.,* aged 7 days, female, was admitted to the hospital in the service of Dr. Stone, on December 17th, 1921. The patient's father, mother and three brothers, aged 7, 12, and 15 years, were all living and well. There was no history of tuberculosis, syphilis, insanity, or hemophilia in the family, and the mother denied any miscarriages or stillbirths.

The patient was a full-term baby, delivered instrumentally, and had not been exposed to any of the acute exanthemata.

At birth the patient was noticeably jaundiced. She had been breast-fed until the day before admission, when she refused to nurse, since which time she had been fed breast milk with a bottle. The patient weighed 9 pounds, 9 ounces at birth. The stools had contained considerable mucus and at times had been gray. During the two days prior to admission, the stools had been black and had contained mucus. The urine had been highly colored since birth. On the day before admission some reddish-blue spots had been noticed on the body which were increasing in size.

Examination revealed a well developed and well nourished female infant weighing 8 pounds and 6 ounces. The skin, even by artificial light, was seen to be markedly jaundiced. There were ecchymoses over the left cheek, both elbows, right knee, and right breast. In the latter location the ecchymotic patch was two inches in diameter. The head was symmetrically shaped without points of tenderness. The sclerae, corneae and conjunctivae were of a yellow color. The pupils reacted to light and accommodation and the extra-ocular movements were well performed. There was no discharge from the ears and no mastoid tenderness. There was no deformity of nor discharge from the nose.

The tongue was dry and along its margin were seen small discrete hemorrhagic areas. The pharyngeal mucous membrane was of normal color and the tonsils showed no evidence of previous or present involvement.

The heart and lungs were negative.

The edge of the liver was felt and percussed two fingers' breadth below the costal margin. Otherwise the abdomen was negative.

The nervous system, skeletal system and glandular system were all negative, and the genitalia and anus were normal.

An admitting diagnosis of congenital obliteration of the bile ducts was made.

On admission 25 c.c. of the father's blood was injected into the patient's buttock.

On December 19th, two days later, the patient had a spontaneous hemorrhage from the umbilical cord, which was clamped and tied after the loss of about one ounce of blood. Two hours later without warning the patient suddenly died.

An autopsy, which was performed five hours after death, revealed the following:

The body was that of a well developed and well nourished white female infant 46 cm. in length. The entire skin, sclerae, conjunctivae and buccal mucosa were of a most pronounced buff orange color. There were patches of ecchymosis varying in diameter from 1.5 to 6 cm. beneath the skin over both elbows, right mastoid region, dorsal surface of the hands, mesial surface of the left leg in its upper third, right patellar region, left internal malleolus, and left sub-scapular region. The umbilicus was about 1 c.m. in length and there was blood clot and small granulations over its distal extremity. Rigor mortis was present but incomplete. There was no post-mortem lividity present. The pupils were equal and measured 4 m.m. in diameter.

There was an absence of free fluid and adhesions in the peritoneal cavity, and the lesser peritoneal cavity was free. The peritoneal surfaces were all moist and glistening, and the organs were all in normal position. The liver extended 4 cm. below the costal border in the right mid-clavicular line, 3 cm. below the costal border in the left mid-clavicular line, and 3 cm. below the ensiform cartilage. The foramen of Winslow was patent, there were no tumor masses or enlarged glands pressing upon the hepatic ducts and vessels, and the latter could be readily recognized and identified *in situ*. The diaphragm extended to the level of the fourth rib on the right side and to the level of the fifth rib on the left. The appendix measured 3 cm. in length and was free. There was no enlargement of the mesenteric lymph nodes.

The thymus weighed 17 grams and was re-

*From the Surgical Service of the Children's Hospital, Boston.

markable only in that it was of a yellowish golden color. There were no enlarged mediastinal lymph nodes. The lungs were collapsed. There was no fluid nor adhesions in the pleural cavities. The pleurae were of a yellowish golden color.

There were no adhesions and but a few c.c. of clear yellowish fluid in the pericardial cavity. The pericardium was of a yellowish golden color.

The heart weighed 33 grams. The epicardium was smooth and glistening and of a yellowish golden color. There was no increase in the amount of epicardial fat. The myocardium was of a pinkish red color tinged with yellow and firm in consistency. The endocardium was smooth and glistening, and of a yellowish golden color except for a small area on the line of closure of the anterior segment of the mitral valve, where there were three minute scattered dark red raised smooth and glistening points, which were evidently foetal vascular remains in the endocardium. Otherwise the valves were normal. The foramen ovale was closed and the coronary orifices were patent.

Measurements: T.V. 4 cm.; P.V. 2 cm.; M.V. 3 cm.; A.V. 2.2 cm.; L.V. 6 m.m.; R.V. 3 m.m.

The combined weight of the lungs was 45 grams. The right lung was smooth and glistening externally and of a yellowish color. It was crepitant throughout. The cut surface was of a yellowish salmon pink color and there were no gross signs of consolidation. The left lung resembled its fellow on the opposite side except that at the apex of the lower lobe there were a few small scattered reddish ecchymoses beneath the visceral pleura.

The spleen weighed 15 grams. Externally it was of a deep magenta color and the capsule was slightly wrinkled. In consistency it was firm. On section it cut with increased resistance and seemed somewhat rubber-like. The cut surface was of a dark brownish red color and the lymph follicles were not visible. The pulp did not scrape.

The entire gastro-intestinal tract was of a yellowish golden color. The intestinal contents were of a grayish color streaked with black. Otherwise it was not remarkable.

The pancreas was of a yellowish golden color, but otherwise not remarkable. The pancreatic duct of Wirsung was patent.

The liver weighed 280 grams. Externally it was smooth and glistening throughout and of a muddy brown color. The shape, relative size of the lobes, and position of the fissures were normal. In consistence it was firm. On section the organ cut with slightly increased resistance and the cut surface was of a muddy brown color with small irregularly shaped patches of a lighter brown scattered throughout. The gall-bladder was collapsed. It was possible to pass a probe from the papilla of Vater both into the gall-bladder and to the liver, thus proving that the common, hepatic, and cystic ducts were patent. There was no foreign body present. When normal saline was injected through a cannula into the common bile duct it was seen that the fluid emerged from the larger intra-hepatic ducts on the cut surface of the liver, thus intimating that the main bile tributaries were patent.

The combined weight of the kidneys was 33 grams. The foetal lobulations of the left kidney were well marked. Its capsule stripped easily, leaving a smooth and glistening muddy brown surface. On section the cortex was of a muddy brown color and measured about 4 m.m. throughout, bearing a normal ratio to the thickness of the medulla. The latter portion was of a yellowish red color. The pelvis and ureter were of a yellowish golden color, but were otherwise not remarkable. The right kidney resembled its fellow on the opposite side in every respect.

The adrenals were somewhat enlarged. On section the left adrenal appeared normal, but in the medullary portion of the right adrenal there was considerable dark red clotted blood.

The genitalia were negative.

The aorta was of a yellowish color, but otherwise negative.

The dura surrounding the spinal cord was of a light golden brown color, but the cord itself appeared normal.

An examination of the head was not permitted.

PATHOLOGICAL HISTOLOGY.

Liver: Microscopically this organ showed a slight increase in the amount of fibrous tissue surrounding the portal areas. It varied slightly in amount in different locations, but not a single portal area had escaped the process. Accompanying this fibrosis, there was a cellular reaction which consisted of relatively large numbers of eosinophiles, together with some mononuclear wandering cells, large and small lymphocytes, and a few polymorphs. This process did not extend in between the liver cells or columns, but remained more or less localized and appeared to produce a crowding of the neighboring liver cells rather than their destruction. The appearance of the bile ducts varied in different fields. Some were definitely patent, with empty gaping lumina; others appeared to be compressed, yet their lumina were patent and empty; while a great many were occluded by casts of inspissated bile. In not one instance, however, was there a flattening of the lining epithelium of the ducts, nor could any actually obliterated ducts be found. Serial sections through the liver showed that though the smaller bile twigs pursued a somewhat tortuous course they finally established a connection with the liver columns. About

some of the central veins there was a fibrous connective tissue increase, accompanied by an occasional eosinophile and lymphocyte, but to a much less marked degree than that seen at the periphery of the lobules.

There was considerable phagocytosis of bile by the endothelial cells and also by some mononuclear phagocytes lying within the sinusoids.

The liver cells themselves showed a marked stippling of their cytoplasm, with basic staining granules of irregular size and shape. Sections stained with Best's carmine stain showed that this latter phenomenon was due to the presence of an excessive amount of glycogen within the cells.

Pancreas: There was an increase in the amount of interstitial tissue separating the acini which amounted to a diffuse cirrhosis of a mild type. This fibrous connective tissue was accompanied by an occasional eosinophile and lymphocyte. The majority of the smaller ducts had their lumina occluded by acid-staining homogeneous colloid-like casts of what was evidently pancreatic secretion, and some of these gave evidence of being distended by the fact that their lining epithelium was flattened. The larger ducts were normal and the cells of the acini and islands were likewise.

Kidneys: The collecting tubules were filled with brownish colloid-like casts, but with the exception of this and a diffuse staining of the tubular cells with bile the organs were normal.

Adrenals: There was a marked degree of hemorrhage into the medullary portion of the right adrenal.

Spinal Cord: This was essentially normal, but remarkable in that it was the only tissue of the body examined which showed no evidence of icterus.

Sections stained by Wolbach's modification of Giemsa stain in order to demonstrate microorganisms in the tissues showed no direct evidence of infection.

Thus, to summarize, a female infant was markedly jaundiced at birth. On the 7th day, she was admitted to hospital and died very suddenly two days later. An autopsy revealed generalized icterus and patulous extra-hepatic duct and gall-bladder. Microscopically the liver showed a biliary cirrhosis and the pancreas a fibrosis.

There are then, with minor variations, seven anatomical possibilities which embrace the condition known as congenital obliteration of the bile ducts, and they are as follows:

I. Obstruction of the hepatic and common ducts; gall-bladder and cystic ducts patent.

II. Obliteration of the gall-bladder and cystic duct; hepatic and common ducts patent.

III. Obliteration of the cystic and hepatic ducts; common duct patent.

IV. Obliteration at a variable point below the junction of the cystic and hepatic ducts.

V. Obliteration of the gall-bladder and cystic, hepatic, and common ducts.

VI. Complete absence of any part or parts of the extra-hepatic biliary apparatus.

VII. Obliteration of the intra-hepatic ducts with patulous gall-bladder and extra-hepatic ducts, *i.e.*, a biliary cirrhosis of the liver.

It can be seen that when the condition is such as exists in Groups II and IV, surgical procedures, if attempted, might be successful in producing a restoration of the normal mechanism. Reports in the literature of such cures are extremely rare, however, owing, perhaps, to the fact that a comparatively small percentage of all cases recorded fall into Groups II and IV, and that the majority were unsuitable for operation, that the accompanying cirrhosis was of such an extent and nature as to cause bile stasis of itself even after the obstruction in the extra-hepatic ducts had been relieved, and that operation was only performed as a last resort when the patient was in a moribund condition. Nevertheless, in view of the otherwise hopeless outlook, it can be reasonably stated that surgical interference is advisable in all cases wherein a positive diagnosis of congenital obliteration of the bile ducts has been made.

In regard to the pathogenesis of the condition, it is interesting to note that Thomson[4] in 1892 regarded the process as arising from a primary congenital malformation of the duct, which caused a catarrh and a complete blocking of the same. This in turn led to a damming back of the bile and a cirrhosis of the liver.

Rolleston,[5] writing in 1905, held that the cirrhosis was the primary condition, and that a cholangitis was produced which descended to the larger ducts and brought about an obliterating fibrosis. He supported his views with the arguments that although there was a constant cirrhosis accompanying obstruction of the bile ducts in infants, in adults cirrhosis of the liver did not accompany aseptic obstruction of the bile ducts, as in the case of carcinoma of the head of the pancreas; also, that the enlarged liver found in these cases resembled the hypertrophic cirrhosis of Hanot; that the spleen was generally found to be enlarged, a feature absent in uncomplicated biliary obstruction; and, finally, that in some instances several cases had been noted to occur in the same family. He still believes that "biliary obstruction *per se* does not constantly cause any form of cirrhosis; but with infection of the obstructed ducts pericholangitis may lead to hepatic fibrosis."[6]

Lavenson,[7] in reporting a case of congenital obliteration of the bile ducts with cirrhosis of the liver, in 1908, made a survey of the literature and came to the following conclusions:

(1) That in the congenital condition, of which the two most prominent features are an obliteration of some portion of the bile ducts and a more or less extensive degree of cirrhosis of the liver, the obliteration of the ducts is the primary condition and the cirrhosis is a result of the ensuing biliary stasis.

(2) That the term "atresia of the bile ducts" better expresses the existing condition than "obliteration of the bile ducts." Lavenson thus stands in direct opposition to the views of Rolleston, whose arguments he attacks by asking why the descending cholangitis is not found more often as a result of the Hanot's cirrhosis in adults, and why the obstruction in infants is most commonly in the hepatic portion of the ducts. This latter fact was not borne out by Howard and Wolbach's thorough analysis, however, as I have already mentioned. Lavenson disregards the enlarged spleen that Rolleston mentions as not having any bearing on the subject, and claims that in a thorough search he could find in the literature but one case in which there was an occurrence of the same disease in one family, and that this had undoubtedly been syphilitic in origin. In support of the congenital malformation theory he shows how faulty union of the two rudimentary portions of the ducts is embryologically possible, and that in a few cases additional congenital defects were noted at autopsy.

For the reason that the rather intricate development of the liver and bile ducts allowed of infinite possibilities in the way of congenital malformation, Holmes, who made the last important contribution on the subject, concluded as follows: "Accumulating evidence tends to show that the condition is usually a developmental anomaly and not the result primarily of inflammatory processes." He believed that the cirrhosis in every instance was a result of the obstruction in the main ducts, and thus regarded Rolleston's theory as lacking in support.

None of the above writers make mention of a case similar to Dunn's nor to the one herein reported by myself, both of which lean towards the likelihood of a non-infectious agent being the etiological factor, and which likewise tend to favor the theory of a cirrhosis being primary to the obliteration of the ducts, for although in cases where congenital obliteration of the extra-hepatic ducts occurs there is a constant accompanying cirrhosis, the converse of the rule on the other hand does not hold true. In other words, congenital cirrhosis of the liver does occur without obliteration of the extra-hepatic ducts.

Doubtless the etiological factor may be either a pure congenital malformation or a pure inflammatory process, or possibly, as might often be the case, a congenital malformation with an inflammatory process grafted on. From the standpoint of treatment and prognosis the matter appears of little import. The fact that a biliary cirrhosis of the liver is constantly present would seem to be the most perplexing factor, for although it is highly probable that this type of cirrhosis is not a progressive one, it is also apparent that in some of its forms, as was found in the case reported above, it is incompatible with life.

To separate congenital biliary cirrhosis of the liver and congenital obliteration of the bile ducts as distinct pathological entities seems unnecessary, since their connection is such an intimate one and so apparent is it that they are the end-result of the same etiological factor or factors, whether found separately or combined. Since the cirrhosis is the constant feature it would almost appear that the term "congenital biliary cirrhosis of the liver" is a more logical appellation for this condition than that of "congenital obliteration of the bile ducts."

CONCLUSIONS.

1. That, from a review of the literature, a mild or severe degree of cirrhosis of the liver constantly accompanies congenital obliteration of the bile ducts.

2. That a congenital biliary cirrhosis of the liver can occur without congenital obliteration of the bile ducts, and is, therefore, not a result of the latter.

3. That in view of the otherwise hopeless outlook, surgical interference is advisable in all cases wherein a positive diagnosis of congenital obliteration of the bile ducts has been made.

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THE PROBLEM OF THE TUBERCULOUS SUSPECT.

BY JOHN B. HAWES, 2ND, M.D., BOSTON.

I HAVE chosen this subject of the "tuberculous suspect" because I believe that it represents a weak point in our endeavors to diagnose tuberculosis in its early stages.

Patients suspected of having tuberculosis may be divided roughly into three classes, only one of which I shall consider here.

The first group comprises many ex-service men who are called, "Tb. suspects." Although they constitute a difficult and trying problem, it is not one which often directly concerns the general practitioner, but is almost entirely in

the hands of the Veterans' Bureau or the Public Health Service.

The second group consists of those patients whom we all are constantly meeting in our private practice. This group is a large one or a small one, according to the diligence and skill of the physician and the impression he is able to make upon his patient as to the seriousness of his case. This group, likewise, I shall not consider here.

The third group to which I would call your attention consists of those patients, — men, women and children, — who attend our out-patient departments and dispensaries and in whom a provisional diagnosis of tuberculosis is made. It is a comparatively small and fortunate few who are given a definite diagnosis on the first visit. I have always maintained that the man who came in to an out-patient department and whose sputum was at once found to be positive to tuberculosis or who had a large hemorrhage while at the clinic might well be considered fortunate, simply because in his case the diagnosis was at once established and adequate treatment instituted. There are many, however,—the great majority indeed,—in whom the diagnosis is not so clear and who are, therefore, asked to return for x-ray examination, and with temperature and pulse records, sputum, etc. In such instances, the diagnosis usually put down on the patient's record is "Ph.?". These patients are always asked to return for further examination, but in far too many instances they do not return. The solution to this problem is not an easy one. The present situation as it exists in my own city is not satisfactory and I believe that the same situation exists elsewhere.

Early in the year 1921, when I became President of the Boston Tuberculosis Association, the first problem that I asked my Executive Committee to undertake was in regard to this point. I had often asked myself what became of the men, women, and children in whom I, for instance, at my clinic at the Massachusetts General Hospital, had made a provisional diagnosis of pulmonary tuberculosis and had asked to come back in a week for further study, but who never came back. What happened to them? Did they go to other dispensaries or to private doctors, or did they drift along until they reached the advanced stages of this disease? In far too many instances, the latter, I fear, was the true answer. At all events, I persuaded my Executive Committee to allow Miss Billings, the Executive Secretary of our Association, and myself to conduct a survey of the city with this point in view. A careful and detailed study was made of all patients in whom there had been a definite diagnosis or a provisional diagnosis of pulmonary tuberculosis at the six large out-patient departments and dispensaries of the city of Boston. The present condition of every one of those patients who came to these out-patient departments from April, 1920, to April, 1921, was investigated.

The following was found to be the situation concerning the tuberculous suspect. Out of a total of 963 patients included in this study there were 415 in whom a provisional diagnosis of pulmonary tuberculosis had been made. From their histories it was evident that the great majority of these had been advised to return for further examination, but that in comparatively few instances had this advice been followed up by home visits, with the result that none of these 415 patients returned for a definite and final diagnosis to the out-patient department in which the provisional diagnosis had been given. There were 140 who afterwards visited some other institution or a private physician and were re-examined; 92, or 69 per cent., of whom were definitely diagnosed as having pulmonary tuberculosis and so reported. Even deducting this group, however, there remains a large number, 338, or 45 per cent. of the original 963 patients, who were strongly suspected of having tuberculosis, but who, so far as could be determined from the records, had never been re-examined or been given a definite diagnosis one way or the other. These patients were not known to the various social service departments of these institutions, nor had they ever been referred to any central office for purposes of record. It is clearly evident that these 338 patients who are now classified as unknown are in urgent need of home visiting and re-examination. This is a group of patients which ought not to exist, and which, if it must exist, should be reduced to the lowest possible figure. The following are two striking examples of what may happen, and indeed what has actually happened to some of these neglected provisional cases.

Case A. This patient was given a provisional diagnosis of pulmonary tuberculosis in an out-patient department July 22, 1920. He was entirely lost track of until reported November 4, 1920, by a private physician. He died 15 days later, November 19, 1920.

[redacted]

Case B. In this case a provisional diagnosis of pulmonary tuberculosis was made at one of the out-patient departments June 15, 1920. He was not heard from again until he was reported by another hospital, April 6, 1921, as having a chronic fibroid phthisis.

At a meeting that I asked Dr. F. X. Mahoney, Health Commissioner of the city of Boston, to call to consider this subject, representatives of the administrative staff and of the social service departments of the six institutions concerned were present. The question was raised as to whether the problem of the tuberculous suspect was really as big as my figures appeared to make it. There was a feeling that after all the majority of these suspects would turn out not

to have consumption. This is a pleasant and optimistic attitude, but, unfortunately, not a sound one. The mere fact that of the 140 suspects in whom the diagnosis was finally settled one way or the other, 69 per cent. turned out to have pulmonary tuberculosis, is sufficient to demonstrate that the problem is a real one.

What are we going to do about it? Various points are absolutely clear and certain to me. In the first place, my investigations demonstrate clearly the advantage of the "one-man" or "two-man" special clinic. The number of patients with a provisional diagnosis who never showed up again was infinitely greater at those general out-patient departments and dispensaries where everything medical is thrown into one large group with doctors in attendance, serving three or four months, than it is in the special clinics where lung cases only are seen, and where the same man or the same group of men are in attendance all the year round. At the clinic of Dr. E. O. Otis, for instance, where, at the Boston Dispensary, he has been in charge for years, there were few such provisional diagnoses, as was also the case, I am glad to say, at my own clinic at the Massachusetts General Hospital.

Next to this, and of no less importance in solving this problem, I would mention the social service departments. Every one of these "Tb. suspects" should be automatically referred to the social service department for home investigation and, particularly, to see that the patient returns for further examination.

Finally, there should be some department or organization which should act as a clearing house to keep track of these patients. I would suggest, for instance, that as soon as such a provisional diagnosis is made, the patient's name and address be recorded at this central office just as positive cases now are. A record of such provisional cases coming from various dispensaries or hospitals in the city would give much more information concerning them than we now have and would prevent much duplication of effort and would permit of their being checked up should they go to another clinic.

The provisional diagnosis of tuberculosis is an unsatisfactory one and one which ought not to exist in large numbers. Some such system as I have outlined above, I believe, will help to reduce the number.

THE EDUCATION OF THE TRAINED NURSE.

BY CHANNING FROTHINGHAM, M.D., BOSTON.

AT the present time there are many problems in regard to trained nurses which are unsettled. It is obvious from studying the different opinions set forth by those interested in the nursing profession that there is no unanimity of opinion in regard to the proper solution for various ones of these problems. The question of the proper type of education for the trained nurse is one that has received considerable attention recently and presents possibly one of the most unsettled points in regard to the nursing profession.

In order to decide what is the proper education for the trained nurse it is important to have a clear conception of just what position the trained nurse should fill in the community. In this regard it is interesting to note the marked change in the possibilities for service which exist for the trained nurse of today in comparison with the trained nurse of only a few years ago, for the nursing profession is a relatively young profession.

At the start the nursing profession called for the training of young women so that they could assist in the care of sick people under the direct supervision of physicians. It was not expected that the trained nurse should assume much, if any, responsibility. At the present time there still exists as perhaps the most important function for the majority of trained nurses the care of the sick in the hospital or the home under the direct supervision of the attending physician. In this position it is not perhaps necessary for the trained nurse to assume much responsibility, nor need she have appreciable knowledge of disease and symptoms, provided the case is so situated that medical attention may always be within easy call.

As, however, medical attention is frequently not available on the instant in many hospitals and homes the nurse even in this capacity must assume more and more responsibility, and in order to do so properly it is advisable for her to have a fair knowledge of certain types of symptoms. Also numerous other opportunities for service exist for the trained nurse today in which she has to work more independently of the physician and has to assume considerably more responsibility. To do this properly the nurse must have more general knowledge of symptoms and disease than if she simply is caring for the sick under supervision. An example is the district nurse who goes out among the people in their homes and who may have to wait several days before a physician is able to visit the home, and who frequently has to decide as to the need for the physician's visit. Another example is the industrial nurse who works in manufacturing establishments and must in many cases assume the responsibility of deciding whether the particular case should see the physician, and also do a considerable amount of minor surgical work on her own initiative. Still another example is the Red Cross nurse who in responding to emergency calls must of necessity assume responsibility because, as she is working at a time of emergency, the probability is that sufficient medical supervision will not be available.

In the field of preventive medicine the trained nurse again has many opportunities for work in which she must assume a certain amount of responsibility and initiative, as, for example, the public health nurse, the dental hygiene nurse, the school nurse and the child welfare nurse. The names attached to the nurses are in themselves explanatory of the character of the work which they do, and no attempt in this short article will be made to go into the details of these various positions, or to enumerate all of them.

The trained nurse of today is frequently trained to be an anesthetist, and experience shows that a nurse trained in the giving of anesthesia with long experience can do it in a much more satisfactory manner than the young physician or medical student who has, perhaps, more theoretical knowledge in anesthesia, but has not had the practical experience. Many surgeons prefer a nurse for an operating assistant. The opportunity for work as laboratory assistants in research work is now open to the trained nurse. All of these positions should be more ably filled by the more broadly educated woman.

In addition to opportunities for work as described above which, although under the supervision of the medical profession, call for the assumption of responsibility and initiative on the part of the nurse, the trained nurse of today must be equipped to take the initiative in certain fields without any supervision, such as the position of teacher in training schools for nurses, and the position of educator of the public in matters of public health and hygiene. Furthermore, trained nurses have been and are successful administrators of hospitals. No attempt will be made to summarize all the possibilities that are open to the trained nurse along these lines at the present time. The ones mentioned above seem to make it clear that the trained nurse of today is called upon for many more different duties than the trained nurse of only a few years ago, and it seems likely that in the future the opportunities for the trained nurse for various types of service will continue to increase.

It is, therefore, quite evident that in educating young women in the nursing profession at the present time it is necessary to train them not only so that they will be equipped to care for sick people under direct supervision of the medical profession, but also so that they will be equipped to act as independent workers in various fields and as educators and leaders in certain positions.

The character of the education of the nurses in the training schools has also been undergoing a change during recent years. There is less drudgery in our better training schools. It is felt that the physical upkeep of the wards belongs to chorewomen and hired help rather than to the pupils of the nursing profession. The hours for the pupils in the schools are shorter, so that there is more opportunity for general mental development. More general knowledge as preliminary to training is required of the pupil nurse, and more general education is given them during their course in many schools. The curriculum in the training schools in regard to general and special medical knowledge has been steadily enlarged. In fact, the question has been seriously considered whether the training school for nurses should be united with the university and at the end of a three or four years' course some degree similar to the Bachelor of Arts should be given.

Of course, all training schools throughout the country have not been able to advance their standards in the same degree, but the trend among the better schools has been in this direction. The result of this change in the education of the trained nurse has been that the nurse of today has a better general education, is better drilled on general health problems, and knows more about disease in addition to her training in the art of nursing than the trained nurse of a few years ago. Like other people who have put in considerable time on education, she expects more financial return per hour for her services than her less well-educated sisters.

Granting that the opportunities for service for the trained nurse of today are more varied than formerly, and also that the method of educating nurses has considerably changed and is still in a transition period, it is important to make a careful analysis of the situation in order to determine if the product of the training school of today is able to supply the needs of the community for the various nursing opportunities which exist. In regard to those opportunities for trained nurses which require leadership, initiative, assumption of responsibility and independent work, there can be no doubt but that the better educated the nurse is who undertakes this work the more successful she will be at it, other things being equal. Therefore the increase in the curriculum for the trained nurse in the better training schools seems to be a step in the right direction toward supplying nurses for these positions.

In regard to those opportunities for trained nurses which consist in care for the sick under supervision, it seems obvious that the better educated the nurse is who does this work the more successfully she will do it. In some quarters it has been suggested that the nurse with the more elaborate training does not do the actual nursing care so well, but it seems as though this must be simply individual variation rather than the result of too much extra knowledge. There seems to be no definite proof that education destroys one's ability in the nursing art, and, therefore, increased education for the nurse should give a better product for this

purpose also. From the viewpoint of the nurse's efficiency, therefore, it seems quite certain that the more highly educated product of our better training schools is better equipped than the nurses trained less well to care for all the needs of the community for trained nurses.

Unfortunately, however, on account of financial reasons, a large number of individuals feel unable to hire these highly educated nurses, who properly demand a larger financial return, and, therefore, today there is a need for nurses to care for those with limited financial resources who become ill. That the less broadly trained woman can care for the sick in a perfectly satisfactory manner under supervision has been amply proved by the past experience in the nursing profession, and, of course, a woman who has not spent so much time in preparation can hardly expect so large a financial return. If, therefore, this highly trained woman, although desirable, is not necessary for the proper care of the sick, and if she is without the reach of many, the trend in regard to the education of nurses is going to leave a need in the community unless some provision is made to supply individuals trained sufficiently to fill this gap.

Assuming for the moment that the preceding summary of the situation in regard to the opportunities for nurses, in regard to the education of nurses, and in regard to the needs of the community for nurses is correct, in what manner should our training schools organize in order to fulfil the needs of the times? The education of the pupil nurse should be kept at the present high plane that it is in our leading schools, with the idea of eventually placing the training school upon a university basis so that the work will lead toward an academic degree of some sort. With this foundation, our best trained nurses will be able to properly fill the numerous positions that are open to them. In addition, it is important that our training schools should turn out a class of women who are trained sufficiently to care for sick people under medical supervision, either in the home or in the hospital.

The details of how to accomplish this must be worked out by those who make a study of the nursing profession. Various possibilities suggest themselves. There might be a fundamental two-year course in nursing, at the completion of which some sort of a title is given to the individual. After the completion of this two years' course a woman can decide whether she will then go out into the world as a practical nurse, to care for the sick, or whether she will continue her studies along some special line, to prepare herself for some of the various fields, open to the trained nurse, which require more elaborate training. Probably at least another two years should be spent in this special preparation and study, and it would be at the end of this two years' work that some academic degree might be given.

Another possibility is the dividing up of the training schools into classes. Those training schools allied with universities and in the larger centers could give a longer course, with considerably more special instruction, with the object of preparing women for the positions that require initiative and leadership. Those schools with less equipment and situated away from these opportunities could offer shorter courses which would train women to care for sick people under supervision. The appropriate titles for these individuals and their relations to the various laws for registration of nurses would require thought and adjustment.

The main points which it has been attempted to emphasize in this short communication are: First, that the opportunities open to the trained nurse at the present time are such that it is important that her education should be extended rather than limited; and second, that although a nurse trained in this manner is probably better suited to care for a sick individual under supervision, she is educated more than is necessary for this work, and also commands a financial return which puts her out of the reach of a great number of people. Therefore it is important for those interested in supplying the community with individuals to care for the sick to provide some type of individual trained well enough to care for the sick person at a price which is within the reach of the great majority of the people.

THE STATES HAVE NOT MET THEIR OBLIGATIONS TO CHILDHOOD.

Notwithstanding the fact that nearly every State has put into its constitution the fundamental principle of the State's obligation in public education, there is not a State in the Union which has yet complied with these plain provisions and given to the boys and girls an equality of opportunity in education. Those who live in the country districts have not been provided facilities for obtaining an education which are in any respect the equal of the facilities which have generally been provided in all populous centers.

There is no other institution in America which has made so little progress in the last century as the rural school. Is this great, rich nation to tolerate this condition of affairs for another century? Or shall we comply with the plain demands which have been determined to be the American policy in education?—Thos. E. Finegan, State Superintendent of Public Instruction, Pennsylvania.

Where the State has bestowed education the man who accepts it must be content to accept it merely as a charity unless he returns it to the State in full in the shape of good citizenship.
Theodore Roosevelt.

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THE MEETINGS OF THE AMERICAN ASSOCIATION FOR THE ADVANCEMENT OF SCIENCE.

The American Association for the Advancement of Science will hold its annual meeting in Boston, beginning on Tuesday, December 26th. With an enrollment of over ten thousand members who represent a great variety of activities, the Association plays an important part in providing a much needed opportunity for the correlation of different branches of scientific work in America. The meeting is of especial interest to the medical profession, for the Association is the only large body in which medical men are brought into direct contact with scientific workers in other fields. The advantages of such an affiliation are well illustrated by the meeting to be held on the afternoon of Friday, December 29th, at which the Sections on Medical Sciences, Entomology, and Parasitology will unite for the discussion of border-line topics which are of interest to all three groups.

The Medical Sciences will be represented by Dr. R. P. Strong, of Harvard University, and Dr. A. B. Macallum, of McGill University, Montreal; Entomology will be represented by Dr. C. T. Brues, of the Bussey Institute, Harvard University, and Dr. L. O. Howard, of the United States Bureau of Entomology; Parasitology will be represented by Dr. C. W. Stiles, of the United States Public Health Service, and Dr. C. A. Kofoid, of the University of California.

It is unusual that so distinguished a group of speakers is found on a single program, and physicians who are interested in the broader aspects of medicine will welcome the chance to hear authoritative statements from leaders in allied branches of science.

PASTEUR.

In the year 1815 Jean Joseph Pasteur, a soldier in the army of Napoleon, a knight of The Legion of Honor, and a farmer by trade, settled in the village of Dôle. On Friday, December 27, 1822, his son Louis was born, a child destined to plough unbroken fields of science and to extend the frontiers of exact knowledge to a degree seldom reached by man.

Louis Pasteur stands alone among the ranks of Humanity's benefactors; the position he attained, even during his lifetime, will be forever secure against the petty storm of hatred, envy, and ignorance that forever seeks to tear down the constructive work of those who are immeasurably greater than their opponents. Of Pasteur's battle in the Academy of Medicine, where the chemist who had solved the mysteries of Farb had continually to defend his ground against the enmity of a profession of which he was not a member—a profession that saw its traditional dogma and doctrine slipping away from it under the searching investigation of this man, many know. That he should have lived to see his great achievement acknowledged and recognized by the country he loved so well to serve, was a reward that falls to the lot of few.

Pasteur's childhood was that of an eager, though not a brilliant, student who sought by every means in his power to gain the knowledge that he felt was so necessary to his advancement, although, at that time, a professorship at Arbois College seemed a reasonable goal for his ambitions. His course at the Ecole Normale, attendance at the Sorbonne Lectures, and the inspiration afforded by J. B. Dumas, later his master and lifelong friend, turned him into a chemist. At the age of twenty-six he revolutionized physical chemistry by discovering the constitution of racemic acid, and gained the lasting interest of Biot, the chemist, then seventy-four years of age. Biot at one time wrote to Pasteur's father, "It is the greatest pleasure that I can experience in my old age to see young men of talent working industriously and trying to progress in a scientific career by means of steady and persevering labour, and not by wretched intriguing."

Pasteur was in 1853 made a knight of The Legion of Honor. In 1856, as a result of the

troubles being experienced by the French brewers, he took up the study of fermentation. This was extended to wines in 1864. The year 1865 was epochal in Pasteur's career, for it was in this year that Dumas asked him to leave the laboratory and undertake the study of the epidemic that had been playing havoc with the silk worm industry since 1849. In 1869 the disease was conquered and immense revenue saved for France, although, the year before, Pasteur had suffered his first paralytic stroke.

The Prussian invasion soon checked investigation in France. Pasteur, unable on account of his paralysis to accompany his colleagues to the front, wrote bitterly, "I wish that France may fight to her last man, her last fortress. I wish that the war may be prolonged until the winter, when, the elements aiding us, all these vandals may perish of cold and distress. Every one of my future works will bear on its title page the words: 'Hatred to Prussia. Revenge! Revenge!'"

Pasteur in 1873 was elected to the Academy of Medicine by a majority of one vote, distrusted still by our profession although Lister had already in 1867 adopted Pasteur's theory of germs, and created antisepsis. It was not until 1877 that antiseptic methods were employed in Paris, despite Pasteur's unremitting advocacy of his cause.

Charbon, splenic fever, or anthrax, exceedingly common among sheep and cattle in France, gave up its mysteries before the experimental method, and successful prophylactic vaccination was discovered. Soon the first experiments on hydrophobia were begun; attenuation of the vision was found possible, and in 1885 Joseph Meister, the little Alsatian lad, became famous as the first human being to receive the Pasteur treatment.

Honor and recognition from all countries had been piling up upon him. He was fêted, welcomed, revered wherever he went. Medals were struck in his honor. Buildings, streets, villages were given his name. The most humble and the most ignorant looked upon him as their benefactor; his opponents became his disciples. Dr. Fleys, head physician of the Aurillac Hospital, said, in proposing a toast to Pasteur, "What the mechanism of the heavens owes to Newton, chemistry to Lavoisier, geology to Cuvier, general anatomy to Bichat, physiology to Claude Bernard, pathology and hygiene will owe to Pasteur. Unite with me, dear colleagues, and let us drink to the fame of the illustrious Pasteur, the precursor of the medicine of the future, a benefactor to humanity."

On November 14, 1888, the Pasteur Institute, built by public subscription among all classes, even little Joseph Meister contributing his share, was inaugurated. In a speech on this occasion M. Christophle remarked that "it might be said that in this public subscription all the virtues flow into unselfishness like rivers into the sea." A jubilee in honor of Pasteur was held at the Sorbonne on his seventieth birthday, on which occasion he was presented with a medal bearing the inscription: "To Pasteur, on his seventieth birthday. France and Humanity grateful."

His work was about over, although his interest remained ever fresh. Diphtheria was being studied. Eleven years before, Klebs had discovered the bacillus, and now the antitoxin was discovered by Behring. The Pasteur Institute immediately began its manufacture, but the leader was failing. In 1894 he had an almost fatal attack of uremia from which he recovered, but the following year his weakness increased, he suffered from a series of paralytic strokes and on September 28, 1895, he died, having lived to see his work succeed and to know that it was good.

DR. BULKLEY'S RETIREMENT FROM THE NEW YORK SKIN AND CANCER HOSPITAL.

According to the New York *Times* the differences of opinion between Dr. L. Duncan Bulkley and the staff of the New York Skin and Cancer Hospital have led to the retirement of Dr. Bulkley. Dr. Bulkley has been outspoken in his opposition to the generally accepted views concerning cancer and has published in the daily papers articles denouncing the arguments in favor of surgery. One of the phrases used in writing on cancer work contained the following words: "a monument to humbuggery and sordid deception."

The hospital governors have issued the following statement:

"In view of the various communications to the lay press of this city by Dr. L. Duncan Bulkley, a member of the medical staff of the New York Skin and Cancer Hospital, the Board of Governors of the hospital feels constrained to make the following statement:

"The Board of Governors and the medical staff of the hospital are not in accord with the theories or the practice of Dr. Bulkley regarding the treatment of cancer. They believe that such practice as he advocates means the loss of valuable time for the patient and by so much diminishes the hope of relief which other methods, advocated and used by the ablest physicians and surgeons throughout the world, do give.

"It is the practice at the New York Skin and Cancer Hospital to use any and all the treatments which research and experience have demonstrated to be of value in such cases.

"In its own research laboratories it is ever seeking knowledge for the treatment, relief and cure of this most dreaded disease.

"Dr. Bulkley is by many years the oldest physician upon our medical staff, but he is no longer in active service at the hospital. The title 'Senior Physician' which he uses has never been authorized by the Board of Governors or by any by-laws of the hospital.

"For the Board of Governors,

"ELIJAH D. MURPHY, *President.*"

Dr. Bulkley is 77 years old, has published books and articles on cancer setting forth his views. His ideas coincide with those expressed by a very small minority of the profession.

Often added years bring to physicians a generous appreciation of the work of those who have studied the same problems and whose reasoning and experience have led to diverse conclusions but occasionally one sees in the aged, inflexibility of mind and a bitterness of spirit wholly inconsistent with scientific ideals. Physicians above all others should exhibit fairness and even tolerance in the discussion of the problems of disease. Rancor only lends weapons to our opponents. It is not evidence of strength, and in this case rather of senility. We regret this exhibition which compelled the hospital governors to take drastic action.

THE ADVENT OF COUÉ.

The intended visit of Coué to this country will once more flood the press with tales of miraculous cures. Apparently the field of therapeusis is wide and free; anyone can enter the lists against the ills of the flesh, and provided his idea has an element of mystery and is untrammeled by the teachings of pathology, he will be sure of a following.

Certain of these fads are less dangerous than others. It is not unlikely, indeed, that those methods of which Couéism may be taken as a type, are beneficial rather than otherwise. There are many people suffering from imaginary ills, or from slight functional disturbances over which they are unnecessarily concerned. For such people, the tonic effect of a course of mental therapeutics is very advantageous. The very fact that numerous sufferers are joined in a common effort to secure health and happiness gives to such healers as Coué a power, through mass psychology, which transcends to a considerable degree the power which may be wielded along similar lines by any orthodox medical man working alone in his office.

Another group which might properly be brought under such a psychological influence, are those afflicted with incurable disease. Surely no one would grudge them the temporary alleviation of their sufferings by their newly aroused hope and courage.

The harmful effect of such a therapeutic revival appears when people suffering from a true pathological condition are led by this will-o'-the-wisp to neglect the help offered by legitimate medicine.

MESSAGE OF DR. LINSLY R. WILLIAMS TO MASSACHUSETTS.

With the opening of the Christmas Seal Sale in Massachusetts, Dr. Linsly R. Williams, president of the National Tuberculosis Association, sends this message to the citizens of the Commonwealth, outlining the situation in Massachusetts as viewed from the conning tower of the great national anti-tuberculosis association. Dr. Williams writes:

"Today Massachusetts is able to point to many fine accomplishments, including a splendid growth in State and local official health agencies. We rejoice with you in these accomplishments, especially in the great reduction in the number of deaths from tuberculosis," and he stated that against 5,291 deaths from this disease in 1911 the number in 1921 was only 3,853, despite the increase in population. While Massachusetts may emphasize its good work accomplished, those interested in public health work should be mindful of the fact that at the present time about 35,000 persons in the State have tuberculosis. The important matters in this connection are, first, that it is necessary to find these persons, and, secondly, a campaign of education must be carried on so that the people themselves may assist in stopping the further spread of this communicable disease. The Health Christmas Seal Sale has for one of its important reasons for being, its high value as an educator of the people.

"For this purpose the Massachusetts Tuberculosis League and its affiliated associations and committees throughout the State are asking for $200,000 at Christmas time through the sale of Christmas Seals. As has often been said, within certain limits public health is purchasable. This applies to individual and community health. The tuberculosis movement in Massachusetts is fortunate in having behind it a body of volunteer workers who have important plans for 1923. Massachusetts has also within its borders the Framingham Tuberculosis and Public Health Demonstration carried on under the auspices of the National Tuberculosis Association. The Demonstration has aroused international interest in the effectiveness of its methods of finding and treating tuberculosis. Massachusetts, therefore, has the workers; and also has the knowledge based on years of experience of how to wage an effective warfare against tuberculosis. All that is needed is the funds with which to carry on the work during the coming year. I am sure that the people of Massachusetts will not fail to appreciate the importance of financing tuberculosis work adequately through the Christmas Seal Sale."

News Notes.

WORCESTER DISTRICT MEDICAL SOCIETY.—The regular meeting was held December 13th, at 4:15 P. M., in the G. A. R. Hall, Pearl street, Worcester. Program: Unilateral Fused Kidney, Dr. Walter D. Bieberbach, Worcester; Slides illustrating the value of Pyelography, Dr. Philip H. Cook, Worcester; The operability of Protastic Obstruction, Dr. J. Dellinger Barney, Boston. Discussion opened by Dr. O. D. Phelps, Worcester.

NOTE.—The committee appointed at the September meeting of the Society to consider the adoption for automobiles, of the A. M. A. emblem, the Caduceus, to take the place of the green cross so commonly used by many cults, wish to make a report at the next meeting in December. The A. M. A. has offered to supply these emblems in quantities not less than one hundred, with the words, "Worcester Distriet," across the lower border of the rim, for $1.20 instead of the regular price of $1.50. The police departments of Worcester and some of the surrounding towns are willing to recognize the emblem and for cars bearing it will make certain allowances in traffic and parking regulations. This will not, however, include repeated and flagrant violations of these regulations by any member of the Society. The A. M. A. will make every effort to limit the sale of these emblems to members of the Society. Will you give your approval or disapproval of the idea by signing and mailing the enclosed card at once?

The Worcester Medical Milk Commission has issued a card setting forth that certified milk is sold in Worcester and gives the names of the producers. A. W. ATWOOD, *Secy.*

THE PETERBOROUGH, N. H., HOSPITAL.—A board of eleven Trustees at Peterborough, New Hampshire, is to have turned over to it next spring a twenty-five-bed institution, in the midst of a ninety-acre tract of land, beautifully situated. The hospital will be very complete and very fine, representing gifts of over $200,000. The trustees are engaged in a study of hospital problems so as to be prepared to provide the best possible service for the people of that section.

WEEK'S DEATH RATE IN BOSTON.—During the week ending December 9, 1922, the number of deaths reported was 223, against 188 last year, with a rate of 15.22. There were 29 deaths under one year of age, against 29 last year. The number of cases of principal reportable diseases were: Diphtheria, 71; Scarlet Fever, 37; Measles, 75; Whooping Cough, 70; Typhoid Fever, 1; Tuberculosis, 25. Included in the above, were the following cases of non-residents: Diphtheria, 14; Scarlet Fever, 9; Measles, 1; Whooping Cough, 1; Tuberculosis, 5. Total deaths from these diseases were: Diphtheria, 3; Scarlet Fever, 1; Measles, 4; Whooping Cough, 4; Typhoid Fever, 1; Tuberculosis, 8. Included in the above were the following cases of non-residents: Diphtheria, 2; Scarlet Fever, 1; Whooping Cough, 1; Typhoid Fever, 1; Tuberculosis, 1.

RABIES IN MAN.—Last year in eight different states there were twelve deaths registered from rabies in man, as follows: California 1, Kentucky 1, Massachusetts 1. New York 4, Ohio 1, Pennsylvania 1, Rhode Island 2, Texas 1.—*Buffalo Sanitary Bulletin.*

RADIUM FOR PARIS.—The city of Paris has authorized the expenditure of 2,500,000 francs (a little less than $200,000) for the purchase of radium for the public hospitals of that city.

ENTRANCE REQUIREMENT OF UNIVERSITY OF PENNSYLVANIA MEDICAL SCHOOL.—Beginning in 1923 applicants for admission to this school must have had three years of college work.

HARVARD MEDICAL SOCIETY.—Meeting in the Peter Bent Brigham Hospital Amphitheatre was held Tuesday evening, Dec. 5, 1922. Program: "Clinical Observations with Henderson's Method of De-etherization," Mr. J. C. White, Harvard Medical School; "Some Remarks on the Lungs in Heart Disease," Dr. C. Lundsgaard, Rockefeller Hospital, New York.

THE COMBINED MEETING OF THE MIDDLESEX SOUTH, NORFOLK AND NORFOLK SOUTH DISTRICTS.

This meeting was held at the Tufts College Medical School Nov. 21st, 1922, and was called to order by Dr. Enos H. Bigelow. Dr. John W. Bartol was the first speaker. He spoke of the responsibility of the profession in matters of legislation affecting public health and the practice of medicine and made a strong plea for more definite interest in the problems before the legislature from time to time.

Dr. James S. Stone discussed the necessity for some extension of the power to license hospitals and explained some of the features of hospital functions which may lead to efforts to have these institutions more generally supervised. He also referred to the work of the Industrial Accident Board in its relation to medical service and called attention to the plans for a special meeting at which speakers would discuss all phases of the care of injured workmen.

Mr. Maurice Caro represented Mr. O'Brien, the district attorney of Suffolk County, and gave an interesting discourse on medical matters from the legal standpoint. About 250 members were present. The meeting was an especially interesting occasion. Refreshments were served after the meeting.

INSTRUCTIVE DISTRICT NURSING ASSOCIATION, BABY HYGIENE ASSOCIATION.

The month of November was characterized by a pronounced and general increase in sickness.

Twenty-six thousand eight hundred and forty-six visits were made by the nurses to 7,720 patients, 2,909 of whom were newly admitted.

This is an increase of 24% in new work over that of November, 1921, a phenomenal jump due not to excessive prevalence of any one disease, but to a notable increase in many.

One of the chief features of the month was the increase in the respiratory diseases, new cases of which rose to 50% more than those of November of last year, the figures being 180 new cases of bronchitis; 135 of pneumonia; 93 of other respiratory diseases. There were also 29 new cases of grippe and 79 of tonsillitis.

Measles also showed an increase, 79 new cases, and whooping cough, 67.

Tuberculosis alone among the chronic diseases showed a slight drop, all the others showing some increase.

Prenatal work has continued to increase, 497 pregnant women being admitted, while more deliveries were attended than during November of last year.

The total number of children now under Baby Hygiene care is 9,366. During the month of November 413 new cases were admitted—an increase of 9% over those of November of last year. Forty-four children were readmitted either at their old stations or at stations in other parts of the city. One hundred and fourteen conferences were held during the month, with a total attendance of 5,010—an average of 44. There was an attendance of 265 at the various classes—posture, nutrition, cooking, etc. Ten thousand two hundred and fifty-six visits were made by nurses and dietitians, and 60 demonstrations were given by the dietitians to individual mothers.

Obituary.

HENRY WHITMAN KILBURN, M.D.

Dr. Henry W. Kilburn, Boston ophthalmologist, died suddenly at Los Angeles, California, December 3, 1922, aged sixty-five.

The son of John and Amanda Maria (Whitman) Kilburn, he was born at Lonsdale, R. I., April 15, 1857. He was a descendant of Thomas Kilburn, who came to this country from Wood Ditton, Cambridgeshire, England, in 1645, and settled in Glastonbury, Conn. Dr. Kilburn was graduated from Harvard in 1880 and from Harvard Medical School in 1884, supplementing his medical course by a year's study of ophthalmology in Berlin, Germany. On his return he was house officer at the Massachusetts Charitable Eye and Ear Infirmary until the spring of 1887. He was ophthalmic surgeon at the Lowell Corporation Hospital for two years, then assistant ophthalmic surgeon at the Boston City Hospital, and finally ophthalmologist-in-chief to the Carney Hospital from 1897 to 1907. His reputation was of the highest, being known as one of the best refractionists in the community. He was a member of the American Ophthalmological Society, the New England Ophthalmological Society, of which he was president for a year, the Boston Society of the Medical Sciences, the Massachusetts Medical Society and the American Medical Association. He belonged also to the Harvard Musical Association and the University, Progressive and Episcopalian Clubs. For many years he lived in West Medford. In 1889 he married Miss Harriet Mason Plumer of Boston.

Dr. Kilburn gave up practice in 1916 and had lived much of the time since in Switzerland, returning to Boston every now and then. His death will be mourned by a large circle of friends.

Miscellany.

A RIFT IN THE CLOUDS.

Frederick Müller, Professor of Medicine in Munich, has been called by many the greatest teacher of medicine in the world. He has done much laboratory work during his career; in fact, his first years were spent in the laboratory of Voit, an older German scientist. Just now, when the Germans (and many Americans) are being criticised widely for lack of humanitarianism in the practice of medicine, the following inspired letter from Munich, signed by Dr. Müller, is distinctly timely:

Dear Dr. Lusk:

You write in a recent letter that Benedict [S. R.] holds it to be an anomaly that I, as a clinician, should concern myself with these physiologic problems. The responsibility for this belongs not alone to my training in Voit's laboratory but also and especially to the circumstance that, as physician at the sick bed, my attention is constantly called to the significance of problems of metabolism, and because

the physiology of metabolism has been stimulated to a remarkable extent through a study of the pathology of metabolism at the bedside of the sick man.

You should read the new book of Petrèn on diabetes. It suggests a number of new problems. On the other hand, I do not believe that the new English experiments on the subject of carbonic acid and oxygen tension in arterial and venous blood will inform us further. We are investigating the blood of the arteries and veins of the arm. The metabolism of the arm and of the hand is of very little importance in comparison with that of the liver and the kidney or even of the heart. Oh, if we could only compare the blood of the aorta with that of the inferior cava and the hepatic vein! The new experiments of Starling are of much greater clinical importance and are fit to establish upon a new foundation our views concerning circulatory disturbances and heart disease.

The clinical teachers are forced to follow the progress made by the pure sciences—chemistry, physics and physiology—because they throw some light upon the processes of disease in man. But we do not approach the sick bed as physiologists, but rather first of all with love toward the sick man and with an intense desire to help him. I believe that this human fundamental element must be inborn or one will never be the right kind of a physician. The clinical teacher must be primarily a good and experienced physician, and not one whose entire interest and experience are of the laboratory. He who does not heartily interest himself in his patient will never be a good clinician. This human, or, if you will, humanitarian, side of our profession is not only the most beautiful but also the most interesting part of it. It assumes an interest not only for the body but also for the mental individuality of the patient, and I can assure you that my afternoon consultation hours, in which I see patients from all the countries of the world, are to me at least as interesting as the work in my laboratory.

Personal contact with the patients during my consultation hours widens my mental horizon not only from a medical but also from an intellectual point of view, for difficult medical cases and interesting personalities from all classes of society come to me during these hours. I therefore find myself out of sympathy with the new American system of "full-time clinicians," which limits the activity of the clinician to a ward in the hospital and forbids private practice among those who do not wish to go to a hospital. I feel that the forbidding of private practice is not in accord with Holy Writ, as expressed in I Timothy, chap. 5, vs. 18.

FRIEDRICH MÜLLER.

Munich, Aug. 10, 1922.

LOW INCIDENCE OF VENEREAL DISEASE IN OUR COLLEGES.

The Buffalo Sanitary Bulletin comments on the results obtained from a recent questionnaire sent by the United States Bureau of Education and the United States Public Health Service to almost one hundred college presidents and executives, asking for their opinions with respect to the prevailing attitudes and practices of college men in the matter of sex.

Sixty-five replies were received, varying greatly in their comments, but the unanimous opinion was that venereal disease in the colleges is of an extremely low incidence; probably much lower than a generation ago.

"The forces responsible for this change, loosely classified, are, first, education, both popular and academic, in matters of health, with an increasing emphasis on the hygiene of sex and venereal diseases; *second*, a more active concern on the part of the college in the physical well-being of its students, including increased opportunities for physical training and play activity; *third*, improvement in environment factors, such as the elimination of the saloon and the suppression of prostitution, and, *fourth*, the influence of co-education upon the 'atmosphere' of the college."

TRYING TO LIFT THE BAN ON MALT LIQUORS.

Edward & John Burke, Limited, of Dublin, bottlers and distributors of Guiness Stout, have filed a complaint in the United States District Court for the Southern District of New York, asking for an injunction to prevent prohibition officers from interfering with the sale of Guiness Stout for medicinal purposes. This complaint is directed against the Willis Campbell Act, in so far as it prohibits the prescribing of stout for medicinal purposes.

In 1904, according to this complaint, answers to questionnaires were received from 435 reputable physicians, "of whom 96 did not prescribe stout as a medicine, and 339, or 78 per cent., stated that in their judgment stout possessed valuable medicinal qualities, and that they habitually prescribed it for their patients, designating the cases in which they felt it was a proper and useful medicine."

We must ourselves confess that we cannot see why stout with an alcoholic content of from 7-8% should be discriminated against in favor of the more potent liquors.

THE INFECTIOUSNESS OF MEASLES.

Dr. F. A. Sharpe, in commenting upon the recent epidemic of measles at Preston, refers to

the extreme infectiousness of this disease. He points out that, when an epidemic breaks out in a district, practically every child in that district, unless naturally immune, falls a victim to that disease.

During the past 50 years measles has been responsible for 1,413 deaths in Preston; 835 have died from whooping cough, 750 from diphtheria, 678 from scarlet fever, 38 from smallpox, while 3,358 have succumbed to epidemic diarrhœa.

Dr. Sharpe emphasizes the need for protecting infants from the infection of measles, since the mortality from this disease is much higher among infants than among older children.—*The Medical Press and Circular.*

COOK PORK WELL TO AVOID TRICHINOSIS.

"Cook pork well" is the advice of the United States Department of Agriculture. Failure to observe this important precaution is liable to be followed by serious illness known as trichinosis. Hogs harboring the parasites show no symptoms and pork containing trichinae is exactly the same in appearance as other pork. No practicable system of meat inspection has been discovered by which persons who eat uncooked or imperfectly cooked pork can be protected from the danger of trichinosis. Cooking destroys the parasites.

The winter season, particularly during the holidays, is when outbreaks of trichinosis are especially likely to occur. At this time of year, smoked and dried sausage and various other products made from pork and eaten without cooking are commonly consumed in considerable quantities in many households, in which the eating of uncooked pork is customary. Entire families may be stricken and as many as a hundred cases of trichinosis have resulted from the meat of a single hog served as uncooked sausage or similar product at some gathering or reunion of people, only those escaping who did not eat any of the uncooked pork. The comparative rarity of the disease may present diagnostic difficulties.

The prevention is obvious and consists in thorough cooking.

Correspondence.

DARWINISM AND EVOLUTION. THEIR RELATION TO THE PHYSICIAN.

East Boston, Mass., Dec. 2, 1922.

Mr. Editor:

The BOSTON MEDICAL AND SURGICAL JOURNAL of November 30th, 1922, contained a few paragraphs under the heading of "Darwinism versus Christianity Again." It referred to a recent conference held by various Protestant clergymen in St. Paul, Minnesota, where it was decided to oppose the teaching of Evolution in the public schools of that state. At this meeting Evolution was spoken of as "antiscriptural and antiscientific theory of the origin of man and the universe."

The JOURNAL then remarks that "although there may be difference of opinion relating to the theories of Evolution it is open to question whether the decision relating to the interpretation of scientific data should be left with the clergy, for there is not sufficient evidence at the present time indicative of an adequate amount of study on the part of the clergy that would warrant leaving the interpretation of the evidence to this body of men. Furthermore, many scientific minds have not found in the theory of Evolution any conflict with religious teaching."

Now it is most important that every physician should have a clear idea of what "Darwinism" and "Evolution" mean. We need not enter into a discussion of Darwin's attitude towards Christianity or the worship of any supernatural being with the hope of future rewards or fear of future punishment. That is beyond the scope of this JOURNAL and does not concern this article.

But Evolution and Darwinism concern not only all physicians but every man and woman who would have an intelligent conception of the origin of our universe. It is surprising to find the large number of medical men who have absolutely no idea of what Evolution means or of the great work accomplished by that great quartette of scientists, Darwin, Huxley, Spencer and Haeckel. Evolution is continually being spoken of by such men as "that monkey theory."

It is the object of this article to briefly outline what we mean by Darwinism and Evolution, with the hope that medical men may extend their knowledge to their further advantage on the subject. A Kentucky legislature, when asked to make a state law, excluding all teaching of Evolution from the public schools, rejected that measure by but one vote. Massachusetts may yet be called upon to decide the question and it behooves the medical fraternity to have at least a fundamental knowledge of the subject.

First, let us ask, how are we going to find out the truth, in so far as it is obtainable, in regard to any and all subjects? What are the methods which we shall adopt? Professor Huxley has left us a formula which is applicable to all propositions. Condensed, it is as follows: "Observe and gather all facts. Experiment with them, classify and compare them, eliminate useless facts, deduct conclusions and then try to verify all conclusions."

Now what do we mean by Evolution? Again, briefly, we mean that all living plants and animals had a common ancestor and originated from one or more simple forms. It means that a unifying principle underlies all phenomena, whether of earth or air, sea or star or human mind. It means organized knowledge for the purpose of utility and for the further acquirement of knowledge.

The idea of Evolution has been in the minds of men for centuries, sages of past time were mindful of it, Greek philosophers guessed at it and the early church of the Christians defended it.

The following incident should be remembered. It is a good one on the theologians. In the year 384, (Christianity now being a state religion and growing in power) the old pagans sent their most distinguished orator, Symmachus, to Milan, to plead with the Christians that they be allowed to retain their old deities.

Behind the throne of the boy Emperor Valentinian, stood Saint Ambrose, the greatest Christian leader since Saint Paul. *And the famous argument by which Ambrose silenced the pagans was in effect the Evolutionary argument.* It was an appeal against conservatism to the constant changefulness and progress of nature.

Ambrose looked round the world for what we should call, in modern language, the laws of nature, and he found the supreme law was change. "Was religion alone," he asked, "to be an exception to the law?" "Were they to cling to old rites and legends when the voice of nature on every side spoke of change, advance, the death of the old, the birth of the new?"

Saint Ambrose won, *but the church, ever since has forgotten his argument.* It has proven too much.

The rhetorical argument of Ambrose has now become a science and the most conspicuous, the most comprehensive, the most illuminating law of nature is Evolution. From the atom of matter to the star, from the little alga swimming in the pond to the orchid, from the worm to the human being, from Niagara to the Alps, from the primitive Bushmen to the civilization of the United States—all was evolved. Religion is no exception.

Men may dispute as to whether things were evolved gradually or by spurts, whether the correct way to conceive the Evolution is Lamarckism, or Weismannism, or Mendelism or Darwinism, but the fact and universality of Evolution remains. All subjects fall under the law and it has revolutionized or profoundly modified every department of human thought and every motive to human action.

The idea of the origin of species by the modification of pre-existent organisms had been in the minds of men long before Darwin.

Linnaeus, Buffon, St. Hilaire, Lamarck, Goethe, Lyell, and Erasmus Darwin had all seen it, but Charles Darwin recognized its universal application where others had seen only the particular.

"Darwinism" refers chiefly to his development of what he calls "Natural Selection," the phrase which has caused so much controversy. He states it as follows, ("Origin of Species" page 74). "This preservation of individual differences and the destruction of those which are injurious, I have called NATURAL SELECTION or the survival of the fittest." It accounted for the development of new species. It did not explain all, the wonder is that it explained so much. Darwin did not expect that it would explain everything, but it has explained so much and been so valuable, that it can never be discarded. The phrase "survival of the fittest" was coined by Herbert Spencer, and meant that those organisms which could best adapt themselves to their environment would live. And "natural selection" meant that the organism retained all useful habits and structures that helped it to survive and discarded all that would prevent it from living.

Professor Huxley in England and Ernst Haeckel in Germany, took up and applied the theory of Evolution to their respective departments—and what happened? Men of science in all lines were obliged to reconstruct old ideas and adapt them to Evolution.

Darwinism and Evolution were thus the great moving causes in a great scientific revolution and in the vast onward movement of the human intellect. By these means, science, which had been in a more or less chaotic maze up to 1860, was placed in an orderly system with a definite plan and recognizable meaning. *And Charles Darwin produced a greater change in current thought than any other man.* He accomplished this by observing nature with a strength of purpose, tenacity, honesty, and ingenuity, never surpassed.

No question can now be considered fairly or completely without looking into its evolutionary aspect. It has opened up a large field for investigation and has placed science on a firm footing; in fact, all modern advancement owes its debt to the idea of Evolution. And without it the science of medicine would still be in the stage of the dark ages.

It is high time that medical men asserted themselves, for they have been asleep too long, especially in matters of education. *The interpretation of the facts of Evolution should be with men trained in the natural sciences, not with theologians.* The minds of dead men of an obscure past should not rule the present or the future unless their teachings have been verified by repeated experiment.

An education in the essentials of science is the one thing most needed by this or any other country. *Verified facts, based on sufficient and best evidence should be sought after.* The doubter, the sceptic, the questioner, all are needed for the advancement of the human race.

No one knows for certain how this universe of ours originated. We have two explanations, one given by theologians and the other by science.

The one given by the former depends upon the guess of primitive and savage man of a low type of mentality to explain the phenomena of nature; the other, Evolution, given by men of science, with trained minds, who have carefully weighed and tested all available evidence to the end that nothing but the truth shall prevail. One leads to mental slavery and retrogression, the other to progress. I believe Saint Ambrose was right.

J. DANFORTH TAYLOR, M.D.

COMMITÉ D'AIDE DE L'UNION DES AVEUGLES DE GUERRE.

25, RUE BALLU, PARIS, (IXe)

Authorized by Governmental decree, April 9, 1921.

Mr. Editor:

I am enclosing a letter from my very good friend Theodore C. Merrill, an American physician now permanently engaged in research work in Paris. I can vouch cordially for Dr. Merrill's good judgment and enthusiasm and also for his earnest work in promoting the Entente Cordiale between American and French physicians. I know that this union for the French war victims who have lost their sight is doing splendid work with terribly limited resources. If there are kind hearted physicians whose eyes may fall upon this letter in the JOURNAL, it is possible they may be induced to contribute to so worthy a cause. On account of my personal knowledge of the great need of this work I shall be especially appreciative if you can give the matter space in the JOURNAL.

Very sincerely yours,
KENDALL EMERSON.
21 High St., Worcester, Mass.

Paris, November 15, 1922.

Dear Colonel Emerson:

I want to ask you kindly to aid and further efforts which I am making in behalf of the Oeuvre indicated in the heading. The Union des Aveugles de Guerre maintains a foyer, or home centre, for the war blinded, where the ex-soldiers may find recreation, a Braille library, aid in securing raw material and employment, and in disposing of their finished articles. Temporary lodging and care are also provided for necessitous cases, and a rest home for the families of the indigent blind is planned. The immediately urgent problem is to keep the centre running.

Coöperating with Doctor de Lapersonne, I am making an appeal to American ophthalmologists and oculists. Doctors de Schweinitz, Wilmer and McReynolds have cordially accorded me their hearty support and I trust that a notice will soon appear in the *Journal of Ophthalmology* and *Journal of the A. M. A.* Doctor William W. Keen has also kindly helped me. If you can kindly bring this matter to the attention of local ophthalmologists, oculists or any others who may be interested, your kindness will be most deeply appreciated by the Union and its blind. You may

note from the heading that I am serving as Delegate for America. I have arranged with the Guarantee Trust Company to receive all funds which I may handle. New York drafts, or certified checks, made in dollors and payable to me, will constitute the best form for transmitting contributions. On the part of the French, efforts will be continued all the time. You are quite familiar with the many needs pressing in France, and that may be left in your experienced hands. Speak a good word for the Union whenever you can, dear sir, and find some people who are able and willing to aid this group of the war blinded, who have unquestionably given highly in the cause of the world's freedom and justice.

Please accept my very best wishes for a happy Christmas and the cordialest of regards from the banks of the Seine.

Most truly yours,

THEODORE C. MERRILL,
Delegate for America of the
Union des Aveugles de Guerre.

10 bis rue Herran, Paris, XVIe.

NEXT MEETING OF THE AMERICAN SURGICAL ASSOCIATION.

Mr. Editor:

I note in THE BOSTON MEDICAL AND SURGICAL JOURNAL of November 30, a statement that the next meeting of the American Surgical Association will be held in Rochester, Minn., in *January, 1923.*

I am not sure of the source of this report, but it is incorrect, as the date of the meeting has been decided only recently, and the meeting will be held in Rochester, Minn., *May 31 and June 1 and 2, 1923.*

Sincerely yours,

R. B. GREENOUGH, *Secretary.*

HUMAN ACTINOMYCOSIS.

December 6, 1922.

Mr. Editor:

I am endeavoring to make a complete study of the distribution of human actinomycosis in this country. The number of cases reported in the literature is surprisingly small, and I know that the disease is not so rare as is sometimes thought. I shall greatly appreciate hearing directly from any one who has had experience with this disease, and desire to know concerning case histories the following: age, sex, occupation, residence, state in which the disease was contracted, location of lesion, duration of symptoms, and any special points of interest connected with the treatment, outcome of the disease, or necropsy findings.

A. H. SANFORD, M.D.

Mayo Clinic, Rochester, Minnesota.

THE TREATMENT OF PNEUMONIA.

December 10, 1922.

Mr. Editor:

I venture to send enclosed clipping in view of your editorial on Pneumonia in your issue of Dec. 7, 1922. I trust you may find it worth reading and reprinting in part. In looking back, I have lost very few cases in private practice, where I was attending physician and patients followed my advice from the beginning.

Yours sincerely,

BEVERLEY ROBINSON.

NOTE:

The clipping* is an editorial analysis of three papers published by Dr. Robinson.

The points made are as follows: Since the pneumococcus is found in the secretions of the mouth and throat of many healthy persons one special indication is for the use of antiseptic gargles with an acid reaction. Second, on the development of chill, fever, pain in the side, cough and expectoration beechwood creosote should be vaporized in the patient's room; third, prevention of contagion; fourth, adequate ventilation; fifth, two nurses; sixth, proper food (mainly milk) with abundance of water; seventh, avoidance of extremes in treatment, especially mentioning digitalis and strychnine.

He believes in the use of quinine, and antimony when the congestion and prexia are prominent features. Alcohol should be used judiciously except in cases of plethora and hepatic engorgment and its effect is good in association with coffee. He also believes in nitroglycerine in cases with marked pulmonary congestion and oedema.

In a later communication especial endorsement is given to the sublingual use of strophanthin.

In a few words he endorses the use of most of the drugs that have been used when definitely indicated except aconite and digitalis.

Medical Record, February 25, 1905.

IN MEMORIAM

LOUIS PASTEUR.

1822—1922.

The milestones of a century of strife
Have passed from sight along this road of time
Since France first offered to mankind a life
That service to mankind has made sublime.

In spite of stiff-backed dogma, worn and old,
In spite of jealousy and hatred blind,
You made the mysteries of earth unfold
Before the patient searchings of your mind.

Made clearer by the light your genius shed,
The light-deflecting crystals you have shown
To have a meaning until then unread,
And Chemistry has claimed you for her own.

The wines that all of France have prized so much,
Regained their sweetness when your goal was won;
The silkworm recognized your magic touch
And at your bidding threads of gold were spun.

As ripples widen in a placid pond,
Your tasks, diversified, still met success.
Disease retreated when you waved your wand,
And grateful nations learned your name to bless.

Pasteur, we hail you in that far beyond
That wisely, still, is veiled from mortal glance.
May gratitude intensify the bond
That grows between America and France!

JOG.

DISEASES REPORTED TO MASSACHUSETTS DEPARTMENT OF PUBLIC HEALTH.

WEEK ENDING DECEMBER 2, 1922.

Disease.	*No. of Cases.*	*Disease.*	*No. of Cases.*
Anterior poliomyelitis	5	Ophthalmia neonatorum	18
Chicken-pox	136	Pneumonia, lobar	111
Diphtheria	244	Scarlet fever	227
Dog-bite requiring anti-rabic treatment	3	Smallpox	1
Encephalitis lethargica	3	Syphilis	31
Epidemic cerebrospinal meningitis	4	Suppurative conjunctivitis	6
German measles	4	Trachoma	6
Gonorrhea	120	Tuberculosis, pulmonary	99
Influenza	7	Tuberculosis, other forms	13
Measles	309	Typhoid	16
Mumps	127	Whooping cough	205
		Hookworm	4

DIABETES AND ITS SURGICAL COMPLICATIONS.

A meeting of unusual interest both to physicians and surgeons is that to be held in the Boston Medical Library on Wednesday, December 27. Our knowledge of diabetes has increased tremendously of late years. The prospect of arresting the disease and of prolonging life had been very bright even before the discoveries of the last few months regarding insulin.

One of the causes of death in diabetes has been the surgical complications. The progress in medical treatment has made possible corresponding progress in the surgical treatment of diabetic lesions.

Improved methods of anesthesia have greatly lessened operative mortality. The ability to get patients sugar free, even for limited periods of time, has rendered possible the healing of operative wounds which oherwise might never have healed. Much more conservative surgery has been made possible.

At this meeting arranged by the Surgical Section of the Suffolk District Society, the chief speaker will be Dr. E. P. Joslin, one of the leading authorities upon diabetes. Following his presentation of the subject representative surgeons from the leading Boston hospitals will summarize their experience in the operative treatment of diabetic lesions.

This meeting, to which all physicians are invited, will teach us what is possible under the improved methods which have already been established. We may get an inkling of what can reasonably be expected from the startling developments of the last few months.

SOCIETY MEETINGS.

DISTRICT SOCIETIES.

A list of society meetings is herewith published. This list will be changed on information furnished by the secretaries of the societies, and will appear in each issue.

Barnstable District: — Hyannis, — **February 2, 1923, (Annual Meeting)**—May 4, 1923.

Bristol South District:—Fall River,—**May 3, 1923.**

Essex North District:—Haverhill, **(Semi-Annual Meeting)**—**January 3, 1923.** Y. M. C. A. Building, **Lawrence, (Annual Meeting)** —May 2, 1923.

Meetings of the Suffolk District and the Boston Medical Library, at the Library:

December 27, 1922:—Surgical Meeting. "Surgical Lesions Occurring in Diabetics: Their Peculiarities and Management," Dr. Elliott P. Joslin, Boston. An account of the experience in this field of the major hospitals of Boston, by members of the staffs.

January 31, 1923:—Medical Meeting. "Epidemic Encephalitis," Dr. E. W. Taylor, Boston.

February 28, 1923:—Medical Meeting. "Colitis," Dr. Henry F. Hewes, Boston.

March 28, 1923:—Surgical Meeting. "A Review of What Surgery Can Accomplish in Diseases of the Thoracic Organs, with a Forecast of the Future," Dr. Howard Lilienthal of New York.

April 25, 1923:—Annual Meeting. Election of Officers. "The Record of the Past Twelve Years in Syphilology, with a Forecast of the Future." A series of 10-minute papers. Dr. C. Morton Smith, Boston, will preside.

The Springfield Academy of Medicine meets the **second Tuesday** of each month. Schedule of speakers includes **the following names:** Dr. Alexis Carrel, Dr. W. B. Long, Dr. J. W. Williams, Dr. W. S. Thayer, and Dr. Barton Cooke, Hist. The date for each speaker has not been assigned.

Middlesex North District:—Meeting, Wednesday, **January 31,** 1923.

Middlesex East District—Jan. 24, 1923. The Nursing Problem. Speaker to be announced later.

March 21, 1923. Mental Factors in Childhood. Paper by Dr. William Healy.

April 18, 1923. Interpretation of Laboratory Findings. Papers by Dr. E. G. Crabtree and one to be announced later.

May 9, 1923. Annual Meeting.

All meetings except the annual meeting will be held at the Harvard Club in Boston. A. E. Small, Secretary.

Worcester District Meetings are scheduled as follows:

January 10, 1923:—**The meeting will be held at the** Worcester State Hospital, Belmont Street, at 4.15 P.M. Programme: "A Discussion of Status Thymico-Lymphaticus and the Inherent Compensatory Possibilities," Dr. Walter Timme, New York City. Discussion will be opened by Dr. W. A. Bryan.

February 14, 1923:—The meeting will be held at the Worcester City Hospital at 4.15 P.M. The programme will consist of a series of papers by members of the staff.

March 14, 1923:—**The meeting will be held at St. Vincent's** Hospital at 8.15 P.M. The programme will consist of a series of papers by members of the staff.

April 11, 1923:—The meeting will be held at Memorial Hospital at 8.15 P.M., and the programme will consist of a series of papers by members of the staff.

May 9, 1923:—Annual meeting and banquet.

STATE, INTERSTATE AND NATIONAL SOCIETIES.

December 26-30, 1922:—American Association for Advancement of Science meets in Boston.

January, 1923:—Massachusetts Society of Examining Physicians (date and place undecided); **Hilbert F. Day, Secretary.** Massachusetts Association of Boards of Health, January 25, Annual Meeting, Boston; W. H. Allen, Mansfield, Mass., Secretary.

January, 1923:—Boston Association of Cardiac Clinics. Meeting January 18, 1923, at 8:15 P.M. Boston Lying-In Hospital (New Hospital). Subject: Pregnancy and Heart Disease.

January, 1923:—Boston Medical History Club will meet January 15, 1923.

February, 1923:—New England Dermatological Society Meeting, **February 14, 1923, at 3.30 P. M.,** in the Skin Out-Patient Department, Massachusetts General Hospital; C. Guy Lane, Secretary.

February, 1923:—Boston Medical History Club will meet the third Monday of this month.

March, 1923:—Massachusetts Society of Examining Physicians (date and place undecided); **Hilbert F. Day, Secretary.**

March, 1923:—Boston Association of Cardiac Clinics. Meeting March 15, 1923, at 8:15 P.M. Boston City Hospital. Subject: Prevention and Relief of Heart Failure.

March, 1923:—Boston Medical History Club will meet the third Monday of this month.

April, 1923:—New England Dermatological Society Meeting, April 11, 1923, at 3.30 P. M., in the Surgical Amphitheatre, Boston City Hospital; C. Guy Lane, Secretary. Massachusetts Association of Boards of Health, April 26, 1923, Boston; W. H. Allen, Mansfield, Mass., Secretary.

April, 1923:—Boston Medical History Club will meet the third Monday of this month.

May, 1923:—Massachusetts Society of Examining Physicians (date and place undecided). American Pediatric Society Meeting, May 31, June 1 and 2, 1923, at French Lick Springs Hotel, French Lick, Ind.; H. C. Carpenter, Secretary.

May, 1923:—Boston Association of Cardiac Clinics. Meeting May 17, 1923, at 8:15 P.M. Children's Hospital. Subject: Rheumatism and Chorea and Heart Disease.

June, 1923:—American Medical Association, **San Francisco, June** 25-29, 1923; Alexander R. Craig,* Chicago, Ill., Secretary.

July, 1923:—Massachusetts Association of Boards of Health. July 26, Nantasket; W. H. Allen, Mansfield, Mass., Secretary.

*Deceased September 2, 1922.

DR. W. T. GRENFELL, superintendent of the Labrador Medical Mission of the Royal National Mission to Deep Sea Fishermen, was recently admitted to the Fellowship of the Royal College of Surgeons, England.—*The London Press and Circular.*

WHY DO THEY LEAVE?—Only 13 of every 100 children entering the first grade of the public schools remain to complete the twelfth grade, or the last year of high school. Of 100 children entering the first grade 86 reach the fifth, 73 the sixth, 64 the seventh, 58 the eighth, 32 the first year of high school, 23 the second year, 17 the third year, and 14 the fourth year, with 13 remaining to graduate.

—[*American Education Week.*